APS Search for 09/123,620
FILE 'USPAT' ENTERED AT 12:21:12 ON 22 MAY 1999

=> e elford h/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	ELFMARK, JIRI/IN
E2	USPAT	3	ELFNER, BO A/IN
E3	USPAT	0 -->	ELFORD H/IN
E4	USPAT	1	ELFORD, ANDREW M/IN
E5	USPAT	3	ELFORD, DAVID/IN
E6	USPAT	8	ELFORD, HOWARD L/IN
E7	USPAT	3	ELFORD, PETER ELLICE/IN
E8	USPAT	1	ELFORD, WILLIAM J/IN
E9	USPAT	1	ELFRING, GARY C/IN
E10	USPAT	4	ELFSTRAND, JAMES K/IN
E11	USPAT	1	ELFSTRAND, STIG OLOF/IN
E12	USPAT	2	ELFSTROM, BO/IN

=> s e6

L1 8 "ELFORD, HOWARD L"/IN

=> d 1-8 bib ab

US PAT NO: 5,366,996 [IMAGE AVAILABLE] L1: 1 of 8
DATE ISSUED: Nov. 22, 1994
TITLE: Method of treating hemoglobinopathies
INVENTOR: **Howard L. Elford**, 3313 Gloucester Rd., Richmond, VA 23227
Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
APPL-NO: 07/986,861
DATE FILED: Dec. 7, 1992
ART-UNIT: 125
PRIM-EXMR: Marianne M. Cintins
ASST-EXMR: M. Moezie
LEGAL-REP: James L. Rowe

US PAT NO: 5,366,996 [IMAGE AVAILABLE] L1: 1 of 8

ABSTRACT:
A therapeutic process for treating anemias in primates, including man, particularly those anemias of genetic origin including sickle-cell anemia, which comprises administering to an anemic primate an amount of a polyhydroxy benzoic, mandelic or phenylacetic acid derivative as specified at a dose level sufficient to increase fetal hemoglobin.

US PAT NO: 5,350,770 [IMAGE AVAILABLE] L1: 2 of 8
DATE ISSUED: Sep. 27, 1994
TITLE: Therapeutic process for the treatment of septic shock
INVENTOR: **Howard L. Elford**, 3313 Gloucester Rd., Richmond, VA 23227
Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
APPL-NO: 07/919,907
DATE FILED: Jul. 28, 1992
ART-UNIT: 125
PRIM-EXMR: Marianne M. Cintins
ASST-EXMR: William R. A. Jarvis
LEGAL-REP: James L. Rowe

US PAT NO: 5,350,770 [IMAGE AVAILABLE] L1: 2 of 8

ABSTRACT:
A therapeutic process for treating septic shock comprising the administration of a polyhydroxy-substituted benzamide or phenylacetamide derivative to a human suffering from, or in danger of contracting, septic shock.

US PAT NO: 5,183,828 [IMAGE AVAILABLE] L1: 3 of 8
DATE ISSUED: Feb. 2, 1993
TITLE: Polyhydroxybenzoic acid derivatives
INVENTOR: Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
Howard L. Elford, 3313 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111
APPL-NO: 07/555,834
DATE FILED: Jul. 20, 1990
ART-UNIT: 125
PRIM-EXMR: Frederick E. Waddell
ASST-EXMR: T. J. Criares
LEGAL-REP: James L. Rowe

US PAT NO: 5,183,828 [IMAGE AVAILABLE] L1: 3 of 8

ABSTRACT:
Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

US PAT NO: 4,942,253 [IMAGE AVAILABLE] L1: 4 of 8
DATE ISSUED: Jul. 17, 1990
TITLE: Polyhydroxybenzoic acid derivatives
INVENTOR: Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
Howard L. Elford, 3343 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111
APPL-NO: 06/907,562
DATE FILED: Sep. 15, 1986
ART-UNIT: 122
PRIM-EXMR: Anton H. Sutto
LEGAL-REP: James L. Rowe

US PAT NO: 4,942,253 [IMAGE AVAILABLE] L1: 4 of 8

ABSTRACT:
Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

US PAT NO: 4,623,659 [IMAGE AVAILABLE] L1: 5 of 8
DATE ISSUED: Nov. 18, 1986
TITLE: Polyhydroxybenzoic acid derivatives
INVENTOR: Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
Howard L. Elford, 3313 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111
APPL-NO: 06/497,370
DATE FILED: May 23, 1983
ART-UNIT: 126
PRIM-EXMR: Natalie Trousof
ASST-EXMR: L. Hendriksen
LEGAL-REP: Charles W. Ashbrook, James L. Rowe

US PAT NO: 4,623,659 [IMAGE AVAILABLE] L1: 5 of 8

ABSTRACT:
Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

US PAT NO: 4,448,730 [IMAGE AVAILABLE] L1: 6 of 8
DATE ISSUED: May 15, 1984
TITLE: Hydroxybenzohydroxamic acids, benzamides and esters and related compounds as ribonucleotide reductase inhibitors
INVENTOR: Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
Howard L. Elford, 3313 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111
APPL-NO: 06/370,023
DATE FILED: Apr. 20, 1982
ART-UNIT: 126
PRIM-EXMR: Paul J. Killos
LEGAL-REP: James L. Rowe, Arthur R. Whale

US PAT NO: 4,448,730 [IMAGE AVAILABLE] L1: 6 of 8

ABSTRACT:
Di, tri and tetrahydroxybenzohydroxamic acids, amides and the corresponding di, tri and tetrahydroxy substituted phenylalkanohydroxamic acids, amides and phenyl esters, ribonucleotide reductase inhibitors.

US PAT NO: 4,394,389 [IMAGE AVAILABLE] L1: 7 of 8
DATE ISSUED: Jul. 19, 1983
TITLE: Hydroxybenzohydroxamic acids, benzamides and esters as ribonucleotide reductase inhibitors
INVENTOR: Bartholomeus van't Riet, 3419 Nobel Ave., Richmond, VA 23222
Howard L. Elford, 3313 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111

APPL-NO: 06/247,171
DATE FILED: Mar. 24, 1981
ART-UNIT: 117
PRIM-EXMR: Thomas A. Waltz
LEGAL-REP: James L. Rowe, Arthur R. Whale

US PAT NO: 4,394,389 [IMAGE AVAILABLE] L1: 7 of 8

ABSTRACT:
Di and trihydroxybenzohydroxamic acids, amides, alkyl substituted amides and phenyl esters, ribonucleotide reductase inhibitors.

US PAT NO: 4,263,322 [IMAGE AVAILABLE] L1: 8 of 8
DATE ISSUED: Apr. 21, 1981
TITLE: Hydroxy benzohydroxamic acids and benzamides
INVENTOR: Bartholomeus van't Riet, 3419 Noble Ave., Richmond, VA 23222
Howard L. Elford, 3313 Gloucester Rd., Richmond, VA 23227
Galen L. Wampler, 6938 Chamberlayne Rd., Mechanicsville, VA 23111
APPL-NO: 06/016,472
DATE FILED: Mar. 1, 1979
ART-UNIT: 117
PRIM-EXMR: Thomas A. Waltz
LEGAL-REP: James L. Rowe, Arthur R. Whale

US PAT NO: 4,263,322 [IMAGE AVAILABLE] L1: 8 of 8

ABSTRACT:
Di or trihydroxybenzohydroxamic acids or N-substituted benzamides, inhibitors or ribonucleotide reductase.

=> s ?hydroxybenzo? or (?hydroxy benzo?)

TERM 'BENZO?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

=> s ?hydroxybenzo? or (?hydroxy (w) (benzohydro? or benzoic or benzoate))

29667 ?HYDROXYBENZO?
151207 ?HYDROXY
273 BENZOHYDRO?
40894 BENZOIC
35208 BENZOATE
3094 ?HYDROXY (W) (BENZOHYDRO? OR BENZOIC OR BENZOATE)
L2 31133 ?HYDROXYBENZO? OR (?HYDROXY (W) (BENZOHYDRO? OR BENZOIC OR BENZOATE))

=> s nf? or (nuclear factor)

15491 NF?
62536 NUCLEAR
268223 FACTOR
205 NUCLEAR FACTOR
(NUCLEAR(W)FACTOR)
L3 15563 NF? OR (NUCLEAR FACTOR)

=> s l2 (p) l3

L4 19 L2 (P) L3

=> d l4 1-19 bib ab kwic

US PAT NO: 5,876,930 [IMAGE AVAILABLE] L4: 1 of 19
DATE ISSUED: Mar. 2, 1999
TITLE: Hybridization assay using self-quenching fluorescence probe
INVENTOR: Kenneth J. Livak, San Jose, CA
Susan J. A. Flood, Fremont, CA
Jeffrey Marmaro, Aurora, CO
Khairuzzaman Bashar Mullah, Union, CA
ASSIGNEE: Perkin-Elmer Corporation, Foster, CA (U.S. corp.)
APPL-NO: 08/558,303
DATE FILED: Nov. 15, 1995
ART-UNIT: 164
PRIM-EXMR: W. Gary Jones
ASST-EXMR: Jezia Riley
LEGAL-REP: Wilson Sonsini Goodrich & Rosati

US PAT NO: 5,876,930 [IMAGE AVAILABLE] L4: 1 of 19

ABSTRACT:
A hybridization assay is provided which uses an oligonucleotide probe which includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of the reporter molecule. The oligonucleotide probe is constructed such that the probe exists in at least one single-stranded conformation when unhybridized where the quencher molecule is near enough to the reporter molecule to quench the fluorescence of the reporter molecule. The oligonucleotide probe also exists in at least one conformation when hybridized to a target polynucleotide where the quencher molecule is not positioned close enough to the reporter molecule to quench the fluorescence of the reporter molecule. By adopting these hybridized and unhybridized conformations, the reporter molecule and quencher molecule on the probe exhibits different fluorescence signal intensities when the probe is hybridized and unhybridized. As a result, it is possible to determine whether the probe is hybridized or unhybridized based on a change in the fluorescence intensity of the reporter molecule, the quencher molecule, or a combination thereof. In addition, because the probe can be designed such that the quencher molecule quenches the reporter molecule when the probe is not hybridized, the probe can be designed such that the reporter molecule exhibits limited fluorescence until the probe is either hybridized or digested.

DETDESC:

DETD(45)
Compound 2: N,N-Diisopropylethylamine (1.1 g, 1.48 mL, 8.52 mmol), 1-**hydroxybenzotriazol** (420 mg, 3.1 mmol) and (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (1.17 g, 3.1 mmol) were added to a stirred solution of **Nfmoc**-.epsilon.-aminocaproic acid (1 g, 2.84 mmol) in DMF (30 mL) at room temperature. After 15 min DL-homoserine (1.35 g, 11.36 mmol). . .

US PAT NO: 5,723,591 [IMAGE AVAILABLE] L4: 2 of 19
DATE ISSUED: Mar. 3, 1998
TITLE: Self-quenching fluorescence probe
INVENTOR: Kenneth J. Livak, San Jose, CA
Susan J.A. Flood, Fremont, CA
Jeffrey Marmaro, Aurora, CO
Khairuzzaman Bashar Mullah, Union City, CA
ASSIGNEE: Perkin-Elmer Corporation, Foster City, CA (U.S. corp.)
APPL-NO: 08/559,405
DATE FILED: Nov. 15, 1995
ART-UNIT: 189
PRIM-EXMR: Ardin H. Marschel
ASST-EXMR: Jezia Riley
LEGAL-REP: Wilson Sonsini Goodrich & Rosati

US PAT NO: 5,723,591 [IMAGE AVAILABLE] L4: 2 of 19

ABSTRACT:
An oligonucleotide probe is provided which includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of the reporter molecule. The oligonucleotide probe is constructed such that the probe exists in at least one single-stranded conformation when unhybridized where the quencher molecule is near enough to the reporter molecule to quench the fluorescence of the reporter molecule. The oligonucleotide probe also exists in at least one conformation when hybridized to a target polynucleotide where the quencher molecule is not positioned close enough to the reporter molecule to quench the fluorescence of the reporter molecule. By adopting these hybridized and unhybridized conformations, the reporter molecule and quencher molecule on the probe exhibit different fluorescence signal intensities when the probe is hybridized and unhybridized. As a result, it is possible to determine whether the probe is hybridized or unhybridized based on a change in the fluorescence intensity of the reporter molecule, the quencher molecule, or a combination thereof. In addition, because the probe can be designed such that the quencher molecule quenches the reporter molecule when the probe is not hybridized, the probe can be designed such that the reporter molecule exhibits limited fluorescence until the probe is either hybridized or digested.

DETDESC:

DETD(48)

Compound 2: N,N-Diisopropylethylamine (1.1 g, 1.48 mL, 8.52 mmol), 1-**hydroxybenzotriazol** (420 mg, 3.1 mmol) and (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (1.17 g, 3.1 mmol) were added to a stirred solution of **Nfmoc**-.epsilon.-aminocaproic acid (1 g, 2.84 mmol) in DMF (30 mL) at room temperature. After 15 min DL-homoserine (1.35 g, 11.36 mmol). . .

US PAT NO: 5,716,628 [IMAGE AVAILABLE] L4: 3 of 19
DATE ISSUED: Feb. 10, 1998
TITLE: Synergistic biocide composition containing pyrithione plus an additive
INVENTOR: Robert T. Vinopal, Mansfield, CT
John D. Nelson, Jr., Bethlehem, CT
Michael W. Glynn, Darien, CT
Robert W. Coughlin, Storrs, CT
Robert F. Vieth, Manchester, CT
Jon R. Geiger, West Hartford, CT
ASSIGNEE: The University of Connecticut, Storrs, CT (U.S. corp.)

APPL-NO: 08/688,136
DATE FILED: Jul. 29, 1996
ART-UNIT: 124
PRIM-EXMR: Paul J. Killos
LEGAL-REP: Dale LynnWiggin & Dana Carlson

US PAT NO: 5,716,628 [IMAGE AVAILABLE] L4: 3 of 19

ABSTRACT:
Disclosed herein is an antimicrobial composition characterized by synergistic antibacterial and antifungal efficacy and comprising a pyrithione salt or pyrithione acid, and at least one compound selected from the group consisting of benzyl and lower alkyl esters of para-hydroxybenzoic acid, salts thereof, carboxylic acids, salts thereof, and combinations thereof. Also disclosed is a method of imparting antimicrobial activity to a composition comprising water or an organic solvent which comprises adding thereto an antimicrobially effective amount of the above-described antimicrobial composition.

DETDESC:

DETD(5)

TABLE 1

Synergistic Antibacterial Effects of Sodium Pyrithione (**NFT**) Mixtures

Test Compound ("TC")	MIC of Mixture (ppm).sup.4 ppm	NPT, Ratio (TC/NPT) Index.sup.b. . .	FIC
*	781	64 >12/1	<0.53
*	391	64 >6/1	<0.52
methyl ester of p-**hydroxybenzoate**	2500	0 --	--
methyl ester of p-**hydroxybenzoate**	625	16 39/1	0.38
methyl ester of p-**hydroxybenzoate**	313	32 10/1	0.38
methyl ester of p-**hydroxybenzoate**	156	32 5/1	0.31
methyl ester of p-**hydroxybenzoate**	78	32 2/1	0.28
methyl ester of p-**hydroxybenzoate**	39	64 1/2	0.52
methyl ester of p-**hydroxybenzoate**	20	64 1/3	0.51
methyl ester of p-**hydroxybenzoate**	10	64 1/6	0.50
none	0	64 --	--
sorbic acid	4096	0 --	--
*	2048	16 128/1	0.75
*	1024	32. . .	

US PAT NO: 5,688,828 [IMAGE AVAILABLE] L4: 4 of 19
DATE ISSUED: Nov. 18, 1997
TITLE: Use of N,N'-bis(mercaptoacetyl) hydrazine derivatives as anticataract agents
INVENTOR: Mark R. Hellberg, Arlington, TX
William H. Garner, Southlake, TX
Jaime E. Dickerson, Jr., Fort Worth, TX
Marjorie F. Lou, Lincoln, NE
ASSIGNEE: Alcon Laboratories, Inc., Fort Worth, TX (U.S. corp.)
APPL-NO: 08/690,610
DATE FILED: Jul. 31, 1996
ART-UNIT: 125
PRIM-EXMR: Zohreh Fay
LEGAL-REP: Michael C. Mayo

US PAT NO: 5,688,828 [IMAGE AVAILABLE] L4: 4 of 19

ABSTRACT:
Compositions containing certain sulfur containing compounds and methods of use in the treatment and prevention of cataracts is disclosed.

DETDESC:

DETD(47)
. . .
%) Purpose

Compound	0.1	active ingredient
Sodium chloride, USP	0.7	tonicity
Boric acid, USP	0.4	preservative
Methyl p-**hydroxybenzoate**, USP	0.002	preservative
Chlorobutanol, USP	0.03	Preservative
Sodium hydroxide, **NF**	q.s.	pH adjustment
Hydrochloric acid, **NF**	q.s.	pH adjustment
Water for injection, USP	q.s.	vehicle

US PAT NO: 5,688,529 [IMAGE AVAILABLE] L4: 5 of 19
DATE ISSUED: Nov. 18, 1997
TITLE: Mycophenolate mofetil high dose oral suspensions
INVENTOR: Deborah Marilyn Lidgate, Los Altos, CA
Li-hua Wang-Kessler, Palo Alto, CA
Bindu Joshi, Milpitas, CA
Sayee Gojanan Hegde, Los Angeles, CA
Leo Gu, Saratoga, CA
ASSIGNEE: Syntex (U.S.A) Inc., Palo Alto, CA (U.S. corp.)
APPL-NO: 08/412,645
DATE FILED: Mar. 29, 1995
ART-UNIT: 152
PRIM-EXMR: Thurman K. Page
ASST-EXMR: James M. Spear
LEGAL-REP: Heller Ehrman White & McAuliffe

US PAT NO: 5,688,529 [IMAGE AVAILABLE] L4: 5 of 19

ABSTRACT:
High dose, dry granulations or powder blends and aqueous oral suspensions of mycophenolate mofetil or mycophenolic acid, contain: active compound (7.5-30%), suspending/viscosity agent, sweetener, flavor, buffer (to a pH of 5-7.5), and optionally contain flavor enhancer, wetting agent, antimicrobial agent and color.

SUMMARY:

BSUM(40)

Antimicrobial agents useful in the formulations of the invention include, for example: sodium benzoate; sodium methyl paraben (preferably **NF**: sodium methyl paraben); methyl paraben (preferably **NF**: methyl paraben, or BP: methyl **hydroxybenzoate**, or EP: methylis **parahydroxybenzoas**); propylparaben (preferably **NF**: propylparaben, or BP/EP: propyl **hydroxybenzoate**); and potassium sorbate (preferably **NF** or BP).

US PAT NO: 5,686,450 [IMAGE AVAILABLE] L4: 6 of 19
DATE ISSUED: Nov. 11, 1997
TITLE: Use of N,N'-bis(mercaptoacetyl) hydrazine derivatives as anticataract agents
INVENTOR: Mark R. Hellberg, Arlington, TX
William H. Garner, Southlake, TX
Jaime E. Dickerson, Jr., Fort Worth, TX
Marjorie F. Lou, Lincoln, NE
ASSIGNEE: Alcon Laboratories, Inc., Fort Worth, TX (U.S. corp.)
APPL-NO: 08/472,452
DATE FILED: Jun. 7, 1995
ART-UNIT: 125
PRIM-EXMR: Zohreh Fay
LEGAL-REP: Michael C. Mayo

US PAT NO: 5,686,450 [IMAGE AVAILABLE] L4: 6 of 19

ABSTRACT:
Compositions containing certain sulfur containing compounds and methods of use in the treatment and prevention of cataracts is disclosed.

DETDESC:

DETD(38)
. . .
%) Purpose

Compound	0.1	active ingredient
Sodium chloride, USP	0.7	tonicity
Boric acid, USP		

0.4 preservative
Methyl p-**hydroxybenzoate**,
0.002 preservative
USP
Chlorobutanol, USP
0.03 Preservative
Sodium hydroxide, **NF**
q.s. pH adjustment
Hydrochloric acid, **NF**
q.s. pH adjustment
Water for injection, USP
q.s. vehicle

US PAT NO: 5,357,636 [IMAGE AVAILABLE] L4: 7 of 19
DATE ISSUED: Oct. 25, 1994
TITLE: Flexible protective medical gloves and methods for their use
INVENTOR: Karl P. Dresdner, Jr., 235 W. 48th St., Apt. #18N, New York City, NY 10036
Kenneth H. Dangman, 400 Riverside Dr., Apt. #1A, New York City, NY 10032
Edward A. Jazlowiecki, 15 Sachems Trail, West Simsbury, CT 06092
APPL-NO: 07/906,829
DATE FILED: Jun. 30, 1992
ART-UNIT: 247
PRIM-EXMR: Clifford D. Crowder
ASST-EXMR: Amy B. Vanatta

US PAT NO: 5,357,636 [IMAGE AVAILABLE] L4: 7 of 19

ABSTRACT:
A flexible protective medical glove containing a non-liquid antiseptic composition and methods for its use are disclosed. The glove comprises a thin inner layer and a thin outer layer of material; preferably the outer layer is a more elastic and less plastic layer than the inner layer. A compartment between the layers of the glove is capable of providing a non-liquid antiseptic composition which comprises an antiseptic in a non-liquid composition. The non-liquid antiseptic composition may also contain a surface-active agent, an algesic agent, a colorant, a vasoconstrictive agent, an odorant, or a viscosity-modifying agent. An object puncturing the glove wall can become coated with the non-liquid antiseptic composition and can automatically transfer some of the antiseptic composition from the glove onto the hand and into a hand wound should the object cause a wound; useful as an immediate preventative antiseptic treatment to help to decontaminate the hand and hand wound of infectious pathogens that may have been transferred there by the object. The treatment can help to protect a gloved individual such as a surgeon, a medical doctor, a health care worker, a law enforcement officer, a dentist or any worker whose work may place them at some risk of becoming contaminated through the hands by an infectious pathogen including the AIDS virus or hepatitis B virus.

DETDESC:

DETD(39)

The . . . chlorhexidine acetate, chlorhexidine hydrochloride, chlorhexidine, other chlorhexidine salts, other hexamethylenebis biguanides, octoxynol, nonoxynol-9, methanol, ethanol, isopropanol, allyl alcohol, rubbing alcohol **NF**, sodium hypochlorite, potassium hypochlorite, calcium hypochlorite, magnesium hypochlorite, sodium dichloroisocyanurate, sodium perborate **NF**, sodium hydroxide, potassium hydroxide, magnesium hydroxide, calcium hydroxide, ammonia, ammonium hydroxide, lithium hydroxide, barium hydroxide, silver hydroxide, other metal hydroxides,. . . eucalyptus oil, glycobiarsol, gramicidin, hexyl resorcinol, methylene blue, peppermint oil, phenylethyl alcohol, phenyl salicylate, methyl salicylate, pine tar, pine oil **NF**, pine oil emulsion, tertiary terpene alcohols, secondary terpene alcohols, alpha-terpineol, borneol, fenchyl alchol, o-methylchavicol, polymixin B sulfate, colistin, chloramphenicol, tetracycline,. . . sulfisoxazole diolamine, sulfacetamide sodium, gentamycin sulfate, amphotericin B, tobramycin, a penicillin, a cephalosporin, salicylic acid, trichloroacetic acid, benzoic acid, pyrogallol **NF** X, pyrogallic acid, sodium benzoate, boric acid, sodium borate, lactic acid, sodium lactate, chloramine, chloramine T, silver nitrate, ammoniacal silver. . . mercuric iodide red, mercuric oxide red, strontium iodide, lithium iodide, magnesium iodide, zinc iodide, silver iodide, selenium iodide, thymol iodide **NF** X, dithymol diiodide, iodinated derivatives of thymol, other iodide salts, povidone-iodine, iodoform, iodinated organic compounds, iodol, iodopyrrol, other iodophors, chlorinated lime, bromide salts, sodium bromide, merbromin **NF**, other bromophors, other brominated chemicals, sodium fluoride and other fluorinated chemicals and fluorophors, Lysol, Nonidet P40, phenyl mercuric acetate, potassium mercuric iodide, proflavine hemisulfate, 3,6-diaminoacridine bisulfate, formaldehyde, glutaraldehyde, parsformaldehyde, butyl **hydroxybenzoate**, mercurous chloride, iodochlorhydroxyquin, zinc nitrate, zinc sulfate, cadmium sulfate, thimerosal **NF**, zinc oxide, zinc acetate, zinc chloride, silver nitrate, silver sulfadiazine, hydrogen peroxide, urea hydrogen peroxide, hydrogen peroxide carbamide, benzoyl peroxide,. . . perchlorite, sodium perchlorite, calcium perchlorite, magnesium perchlorite, zinc perchlorite, zinc peroxide, zinc carbonate, zinc hydroxide, zinc sulfate, succinyl peroxide, succinchlorimide **NF** IX, N-Chloro-succinimide, potassium permaganate, sodium chlorate, potassium chlorate, phenol, sodium phenolate, domiphen bromide, salicylic acid, bismuth-formic-iodide, bismuth subgallate, bacitracin zinc,. . . hydroxynalidixic acid, pipemidic acid, norfloxacin, norfloxacin hydrochloride, other quinolones, 8-hydroxyquinoline sulfate, sodium phenolate, thyme oil, o-cresol, m-cresol, metacresylacetate, p-cresol, cresol **NF**, 4-chloro-m-cresol, 4-chloro-S,5-xylenol, saponified cresol solution **NF**, methylphenol, ethyl phenol, other alkyl phenols, o-phenyl phenol, other aryl phenols, bis-phenols, phenyl-mecuric chloride, phenylmecuric borate, resorcinol, resorcinol monoactetate **NF**, orthophenylphenol, chloroxylenol, hexyl-resorcinol, parachlorophenol, paratertiary-amylphenol, thymol, chlorothymol **NF**, menthol, butylparaban, ethylparaben, methylparaben, propylparaben, triclosan, bithionol **NF**, o-benzyl-p-chlorophenol, hexachlorophene, poloxamer 188, benzalkonium chloride where the alkyl groups attached to the nitrogen represent any alkyl from CH.sub.3 to. . . C.sub.18 H.sub.37, methylbenzethonium chloride, cetrimonium bromide, abikoviromycin, acetylenedicarboxamide, acetyl sulfamethoxypyrazine, triclobisonium chloride, undecoylium chlorideiodine, coal tar solution, furazolidone, nifuroxime, nitrofurazone **NF**, nitromersol **NF**, oxychlorosene, sodium oxychlorosene, parachlorophenol **NF**, camphorated parachlorophenol **NF**, phenylmercuric nitrate **NF**, gentian violet USP, hexamethylpara-rosaniline chloride, rosaniline chloride, pentamethylpararosaniline chloride, methylrosaniline chloride, tetramethylpararosaniline chloride, nonylphenoxypolyethoxyethanol, methoxypolyoxyetheneglycol 550 laurate, oxyquinoline benzoate, p-triisopropylphenoxypolyethoxy-ethanol, halazone **NF**, dichloramine-T, benzethonium chloride, econazole, cetylpyridinium chloride, methylbenzethonium chloride, cetyldimethylbenzylammonium chloride, dichlorobenzalkonium chloride, domiphen bromide, triclocarban, clotrimazole, ciclopirox olamine, undecylenic acid,. . . acid acriflavine, 5-aminoacridine hydrochloride monohydrate, malachite green G, dodecyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, dequalinium chloride BP, dibromopropamidine isethionite, hexadecyltrimethylammmonium bromide, chloroazodin **NF** X, N-chloro-p-toluenesulfonamidosodium, 4-[(dichloroamino)sulfonyl]-benzoic acid, methenamine, methenamine mandelate, methenamine hippurate, octoxynol 9, phenazopyridine hydrochloride, 9-aminoacridine hydrochloride, bismuth tribromophenate, p-tert-butylphenol, cetyldimethylethylammonium bromide,. . .

CLAIMS:

CLMS(5)

5. . . . from the group consisting of chlorhexidine gluconate, chlorhexidine acetate, chlorhexidine hydrochloride, octoxynol, nonoxynol-9, methanol, ethanol, isopropanol, allyl alcohol, rubbing alcohol **NF**, sodium hypochlorite, potassium hypochlorite, calcium hypochlorite, magnesium hypochlorite, sodium dichloroisocyanurate, sodium perborate **NF**, sodium hydroxide, potassium hydroxide, magnesium hydroxide, calcium hydroxide, ammonia, ammonium hydroxide, lithium hydroxide, barium hydroxide, silver hydroxide, sodium tetradecyl sulfate,. . . eucalyptus oil, glycobiarsol, gramicidin, hexyl resorcinol, methylene blue, peppermint oil, phenylethyl alcohol, phenyl salicylate, methyl salicylate, pine tar, pine oil **NF**, alpha-terpineol, borneol, fenchyl alcohol, o-methylchavicol, polymixin B sulfate, salicylic acid, trichloroacetic acid, benzoic acid, pyrogallol **NF** X, pyrogallic acid, sodium benzoate, boric acid, sodium borate, lactic acid, sodium lactate, ohiofamine, chloramine T, silver nitrate, ammoniacal silver. . . mecuric iodide red, mecuric oxide red, strontium iodide, lithium iodide, magnesium iodide, zinc iodide, silver iodide, selenium iodide, thymol iodide **NF** X, dithymol diiodide, povidone-iodine, iodoform, iodol, iodopyrrol, chlorinated lime, potassium bromide, sodium bromide, merbromin **NF**, sodium fluoride, potassium fluoride, phenyl mercuric acetate, potassium mecuric iodide, proflavine hemisulfate, 3,6-diaminoacridine bisulfate, formaldehyde, glutaraldehyde, paraformaldehyde, butyl **hydroxybenzoate**, mercurous chloride, iodochlorhydroxyquin, zinc nitrate, zinc sulfate, cadmium sulfate, thimerosal **NF**, zinc oxide, zinc acetate, zinc chloride, silver nitrate, silver sulfadiazine, hydrogen peroxide, urea hydrogen peroxide, hydrogen peroxide carbamide, benzoyl peroxide,. . . perchlorite, sodium perchlorite, calcium perchlorite, magnesium perchlorite, zinc perchlorite, zinc peroxide, zinc carbonate, zinc hydroxide, zinc sulfate, succinyl peroxide, succinchlorimide **NF** IX, N-Chlorosuccinimide, potassium permanganate, sodium chlorate, potassium chlorate, phenol, camphorated phenol, phenol glycerin, chloroxylenol, 4-chloro-3,5-xylenol, sodium phenolate, domiphen bromide, salicylic. . . zinc sulfocarbolate, hydroxynalidixic acid, pipemidic acid, norfloxacin, norfloxacin hydrochloride, 8-hydroxyquinoline sulfate, sodium phenolate, thyme oil, o-cresol, m-cresol, metacresylacetate, p-cresol, cresol **NF**, 4-chloro-m-cresol, 4-chloro-3,5-xylenol, saponified cresol solution **NF**, methylphenol, ethyl phenol, other alkyl phenols, o-phenyl phenol, other aryl phenols, bisphenols, phenyl-mecuric chloride, phenylmecuric borate, resorcinol, resorcinol monoactetate **NF**,

orthophenylphenol, chloroxylenol, hexylresorcinol, parachlorophenol, paratertiary-amylphenol, thymol, chlorothymol **NF**, butylparaban, ethylparaben, methylparaben, propylparaben, triclosan, bithionol **NF**, o-benzyl-p-chlorophenol, hexachlorophene, poloxamer 188, a benzalkonium chloride wherein the alkyl groups attached to the nitrogen represent an alkyl from CH.sub.3 to C.sub.18 H.sub.37, triclobisonium chloride, undecoylium chlorideiodine, coal tar solution, furazolidone, nifuroxime, nitrofurazone **NF**, nitromersol **NF**, oxychlorosene, sodium oxychlorosene, parachlorophenol **NF**, camphorated parachlorophenol **NF**, phenylmercuric nitrate **NF**, gentian violet USP, hexamethylpara-rosaniline chloride, rosaniline chloride, pentamethylpararosaniline chloride, methylrosaniline chloride, tetramethylpararosaniline chloride, nonylphenoxypolyethoxyethanol, methoxypolyoxyetheneglycol 550 laurate, oxyquinoline benzoate, p-triisopropylphenoxypolyethoxy-ethanol, halazone **NF**, dichloramine-T, benzethonium chloride, econazole, cetylpyridinium chloride, methylbenzethonium chloride, cetyldimethylbenzylammontum chloride, dichlorobenzalkonium chloride, domiphen bromide, triclocarban, clotrimazole, ciclopirox olamine, undecylenic acid,. . . acid acr]flavine, 5-aminoacridine hydrochloride monohydrate, malachite green G, dodecyltrimethylammonium bromide, tetradecyltrimethyl-ammonium bromide, dequalinium chloride BP, dibromopropamidine isethionite, hexadecyltrimethylammmonium bromide, chloroazodin **NF** X, N-chloro-p-toluenesulfonamidosodium, 4-[(dichloroamino)sulfonyl]-benzoic acid, methenamine, methenamine mandelate, methenamine hippurate, octoxynol 9, phenazopyridine hydrochloride, 9-aminoacridine hydrochloride, bismuth tribromophenate, p-tert-butylphenol, cetyldimethylethylammonium bromide,. . .

US PAT NO: 5,082,651 [IMAGE AVAILABLE] L4: 8 of 19
DATE ISSUED: Jan. 21, 1992
TITLE: Pharmaceutical compositions
INVENTOR: John N. C. Healey, Hitchin, England
Marshall Whiteman, Baldock, England
ASSIGNEE: Smith Kline & French Laboratories Limited, Welwyn Garden City, England (foreign corp.)
APPL-NO: 07/514,634
DATE FILED: Apr. 25, 1990
ART-UNIT: 125
PRIM-EXMR: Shep K. Rose
LEGAL-REP: Linda E. Hall, Stuart R. Suter, Edward T. Lentz

US PAT NO: 5,082,651 [IMAGE AVAILABLE] L4: 8 of 19

ABSTRACT:
Pharmaceutical compositions suitable for intra-rectal administration in the form of a foam are described which comprise a therapeutically effective amount of 5-aminosalicylic acid, a pharmaceutically acceptable aqueous carrier therefor, and means for generating a foam.

DETDESC:

DETD(2)
. . .
PROPELLANT)

	Weight % (w/w)	(g)
5-Aminosalicylic Acid	15.0	150.0
Polysorbate 80	0.25	2.5
Emulsifying Wax (`Polawax **NF**`)	0.5	5.0
Colloidal Silicon Dioxide (`Aerosil 200`)	0.5	5.0
Sodium Metabisulphite	0.3	3.0
Disodium Edetate, dihydrate	0.1	1.0
Methylparahydroxybenzoate	0.2	2.0
Propylparahydroxybenzoate	0.04	0.4
Disodium Hydrogen Orthophosphate, 12H.sub.2 O	1.19	11.9
Sodium Dihydrogen Orthophosphate, 2H.sub.2 O	0.52	5.2
Glycerol. . .		

DETDESC:

DETD(3)
. . .

	% (w/w)	(g)
5-Aminosalicylic Acid	25.0	150.0
Sorbitan mono-oleate (`Span 80`)	0.25	1.5
Emulsifying Wax (`Polawax **NF**`)	0.5	3.0
Colloidal Silicon Dioxide (`Aerosil 200`)	0.5	3.0
Sodium Metabisulphite	0.3	1.8
Disodium Edetate, dihydrate	0.1	0.6
Methylparahydroxybenzoate	0.2	1.2
Propylparahydroxybenzoate	0.04	0.24
Disodium Hydrogen Orthophosphate, 12H.sub.2 O	1.19	7.14
Sodium Dihydrogen Orthophosphate, 2H.sub.2 O	0.52	3.12
Glycerol. . .		

DETDESC:

DETD(4)
. . .
CONCENTRATE
(without Addition of Propellant)

	Weight % (w/w)	(g)
5-Aminosalicylic Acid	25.0	250.0
Emulsifying Wax (`Polawax **NF**`)	0.75	7.5
Sodium Metabisulphite	0.3	3.0
Disodium Edetate, dihydrate	0.1	1.0
Methylparahydroxybenzoate	0.2	2.0
Propylparahydroxybenzoate	0.04	0.4
Disodium Hydrogen Orthophosphate, 12H.sub.2 O	1.19	11.9
Sodium Dihydrogen Orthophosphate, 2H.sub.2 O	0.52	5.2
Water. . .		

DETDESC:

DETD(6)
. . .
FOAM

	Weight % (w/w)	(g)
5-Aminosalicylic Acid	25.0	250.0
Polysorbate 80	0.25	2.50
Emulsifying Wax (`Polawax **NF**`)	0.5	5.0
Colloidal Silicon Dioxide (`Aerosil 200`)	0.5	5.0
Sodium Metabisulphite	0.3	3.0
Disodium Edetate, dihydrate	0.1	1.0
Methylparahydroxybenzoate	0.2	2.0
Propylparahydroxybenzoate	0.04	0.4
Disodium Hydrogen Orthophosphate, 12H.sub.2 O	1.19	11.9
Sodium Dihydrogen Orthophosphate, 2H.sub.2 O	0.52	5.2
Glycerol. . .		

DETDESC:

DETD(7)
. . .

%	Weight (w/w) (g)
5-Aminosalicylic Acid	22.50 2.475
Polysorbate 20 (Tween 20)	10.00 1.100
Emulsifying Wax (`Polawax **NF**`)	0.40 0.044
Colloidal Silicon Dioxide (Aerosil 200)	0.40 0.044
Sodium Metabisulphite	0.30 0.033
Disodium Edetate, dihydrate	0.10 0.011
Methylparahydroxybenzoate	0.20 0.022
Propylparahydroxybenzoate	

0.04 0.0044
Disodium Hydrogen Orthophosphate, 12H.sub.2 O
1.19 0.131
Sodium Dihydrogen Orthophosphate, 2H.sub.2 O
0.52 0.057
Glycerol. . .

US PAT NO: 5,041,280 [IMAGE AVAILABLE] L4: 9 of 19
DATE ISSUED: Aug. 20, 1991
TITLE: Toothpaste composition for stain removal
INVENTOR: Irwin E. Smigel, New York, NY
ASSIGNEE: Epilady USA, Inc., Culver City, CA (U.S. corp.)
APPL-NO: 07/103,533
DATE FILED: Oct. 1, 1987
ART-UNIT: 189
PRIM-EXMR: F. T. Moezie
LEGAL-REP: Darby & Darby

US PAT NO: 5,041,280 [IMAGE AVAILABLE] L4: 9 of 19

ABSTRACT:
A toothpaste composition having the following ingredients, by weight:

Dicalcium Phosphate dihydrate:
From 1.0% to 50%
Calcium Carbonate From 1.0% to 50%
Sodium Bicarbonate From 1.0% to 50%
Magnesium Carbonate From 1.0% to 25%
Sorbitol 70% From 1.0% to 50%
Corn Starch From 0.5% to 10%
Cellulose Gum From 0.5% to 5.0%
Calcium Peroxide From 0.5% to 5%
Lathanol LAL (Sodium Lauryl
From 0.1% to 5%
Sulfoacetate)
Aluminum Hydroxide From 0.01 to 1%
Saccharinate (Sodium Salt)
From 0.05% to 2%
Flavoring material From 0.05% to 2%
Alkylparaben From 0.05% to 1.0%
Sodium monofluorophosphate
From 0.70% to 0.80%
Titanium Dioxide From 0.1% to 10%
Deionized Water From 10% to 50%

DETDESC:

DETD(7)
. . .
0.7
Aluminum Hydroxide 0.1
Saccharinate (Sodium Salt)
0.5
Flavoring Material 1
Consisting of:
Menthol crystals 20%
Oil of Spearmint **NF**
20%
Terpeneless Spearmint
30%
Oil of Peppermint 20%
Oil of Anise (imitation)
10%
Methylparaben 0.5
(Hydrobenzoic acid methyl ester)
Propylparaben 0.03
(**Hydroxybenzoic** acid propylester)
Sodium Monofluorophosphate
0.76
Titanium Dioxide 1.0
Deionized Water (to make up 100%)
47.46

US PAT NO: 4,898,728 [IMAGE AVAILABLE] L4: 10 of 19
DATE ISSUED: Feb. 6, 1990
TITLE: Process for production of composition containing lecithin and polyvinylpyrrolidone
INVENTOR: Robert R. Vartan, Bristol, TN
ASSIGNEE: Beecham Group p.l.c., England (foreign corp.)
APPL-NO: 07/178,487
DATE FILED: Apr. 7, 1988
ART-UNIT: 155
PRIM-EXMR: Joseph L. Schofer
ASST-EXMR: Carmen B. Pili-Curtis
LEGAL-REP: Jacobs & Jacobs

US PAT NO: 4,898,728 [IMAGE AVAILABLE] L4: 10 of 19

ABSTRACT:
A process for the production of a sterile composition containing lecithin and polyvinyl pyrrolidone is disclosed in which the lecithin and polyvinyl pyrrolidone, optionally with one or more preservative powders are admixed in a solvent comprising about 75% to 90% methyl isobutyl ketone and about 10% to 25% isopropyl alcohol, and the solution passed through a millipore filter in order to render the ingredients sterile. The process is usefully employed in the production of injectable compositions of amoxycillin and ampicillin.

SUMMARY:

BSUM(11)

Preferably . . . are also dissolved in the MIBK/IPA solvent system in processes of the invention. A preferred preservative is an ester of p-**hydroxybenzoic** acid, and in particular a mixture of methyl p-hydroxybnnzoate and propyl p-**hydroxybenzoate**. A commercial source of these preservative powders are known as methylparaben **NF** and propylparaben **NF** respectively.

US PAT NO: 4,883,805 [IMAGE AVAILABLE] L4: 11 of 19
DATE ISSUED: Nov. 28, 1989
TITLE: Stable, Injectable solutions of vinca dimer salts
INVENTOR: Rodney Kasan, Raanana, Israel
Haim Yellin, Ramat-Gan, Israel
Michael Seiffe, Raanana, Israel
ASSIGNEE: Teva Pharmaceutical Industries Ltd., Israel (foreign corp.)
APPL-NO: 07/078,805
DATE FILED: Jul. 28, 1987
ART-UNIT: 118
PRIM-EXMR: William R. Dixon, Jr.
ASST-EXMR: James M. Hunter
LEGAL-REP: Steinberg & Raskin

US PAT NO: 4,883,805 [IMAGE AVAILABLE] L4: 11 of 19

ABSTRACT:
A stable, injectable pharmaceutical composition of vinca dimer salts. The compositions are in the form of an aqueous solution comprising per 1 ml of solution:
from about 0.2 to about 2 mg of one or more pharmaceutically acceptable vinca dimer salts;
from about 0.1 to about 1.0 mg of a pharmaceutically acceptable ethylenediamine-tetraacetic acid (EDTA) salt;
acetate buffer in an amount necessary to maintain said aqueous solution at a pH of from about 3.0 to about 5.5; and
from about 1.5 to about 2.5 mg of a preservative selected from methyl paraben, propyl paraben and mixtures thereof.

DETDESC:

DETD(28)

Materials

Vincristine sulfate BP/USP
Plantex, Israel
Methyl **hydroxybenzoate** BP/**NF**
Machteshim, Israel
(methyl paraben)
Propyl **hydroxybenzoate** BP/**NF**
Machteshim, Israel
(propyl paraben)
Edetate disodium BP/USP
Merck, Germany
Sodium Acetate 3H.sub.2 O BP/USP
Merck, Germany
Acetic acid BP/**NF** Merck, Germany

US PAT NO: 4,777,050 [IMAGE AVAILABLE] L4: 12 of 19
DATE ISSUED: Oct. 11, 1988
TITLE: Controlled-release dosage form comprising acetaminophen, pseudoephedrine and dexbrompheniramine
INVENTOR: Winston A. Vadino, Whitehouse Station, NJ
ASSIGNEE: Schering Corporation, Kenilworth, NJ (U.S. corp.)
APPL-NO: 07/029,032
DATE FILED: Mar. 23, 1987
ART-UNIT: 139
PRIM-EXMR: Michael R. Lusignan
LEGAL-REP: Anita W. Magatti, Stephen I. Miller, James R. Nelson

US PAT NO: 4,777,050 [IMAGE AVAILABLE] L4: 12 of 19

ABSTRACT:
The invention relates to a controlled release dosage form comprising three actives: acetaminophen, pseudoephedrine and dexbrompheniramine.

DETDESC:

DETD(8)

Ingredients	Approximate g/Batch	mg/tablet
Hydroxypropyl Methylcellulose 2910 or 2906 USP	1,440	12
Polyethylene glycol 3350 **NF**	300	2.5
Methyl p-**hydroxybenzoate** **NF**	14.4	0.12
Propyl p-**hydroxybenzoate** **NF**	10.8	0.09
Purified Water USP (evaporates)	(1)	--
Coloring Agent	(2)	--

(1) Sufficient amounts of. . .

US PAT NO: 4,690,776 [IMAGE AVAILABLE] L4: 13 of 19
DATE ISSUED: Sep. 1, 1987
TITLE: Method of manufacture of a toothpaste composition
INVENTOR: Irwin E. Smigel, 635 Madison Ave., New York, NY 10022
APPL-NO: 06/817,043
DATE FILED: Jan. 8, 1986
ART-UNIT: 223
PRIM-EXMR: Richard D. Lovering
LEGAL-REP: Roberts, Spiecens & Cohen

US PAT NO: 4,690,776 [IMAGE AVAILABLE] L4: 13 of 19

ABSTRACT:
A method of preparing a toothpaste composition by the steps of adding calcium phosphate in an amount of 0.5 to 5% by weight of the composition and sodium perborate in an amount of 0.5 to 5% by weight of the composition to hot water to form a first mixture and agitating the first mixture, adding to the first mixture sorbitol in an amount of 1 to 50% by weight of the composition, cornstarch in an amount of 0.5 to 10% by weight of the composition and aluminum hydroxide in an amount of 0.01 to 1% by weight of the composition to form a second mixture and agitating the second mixture, adding to the second mixture dicalcium phosphate in an amount of 1 to 50% by weight of the composition and sodium monofluoride phosphate in an amount of 0.7 to 0.8% by weight of the composition to form a third mixture and agitating the third mixture, adding to the third mixture sodium bicarbonate, in an amount of 1 to 50% by weight of the composition, gradually adding increments of a flavoring material in an amount of 0.05 to 2% to control any foaming and to facilitate release of gases to form a fourth mixture, and adding to the fourth mixture sodium lauryl sulfoacetate in an amount of 0.1 to 5% and gum in an amount of 0.5 to 5% and agitating the fourth mixture until a homogeneous paste composition is obtained.

SUMMARY:

BSUM(36)

. . .
Aluminum Hydroxide 0.1
Saccharinate (Sodium Salt) 0.5
Flavoring Material 1
Consisting of:
Menthol crystals 20%
0.1 of Spearment **NF** 20%
Terpeneless Spearmint 30%
Oil of Peppermint 20%
Oil of Anise (imitation) 10%
Methylparaben 0.5
(**Hydroxybenzoic** acid methyl ester)
Propylparaben 0.03
(**Hydroxybenzoic** acid propylester)
Sodium Monofluoride Phosphate 0.76
Titanium Dioxide 1.0
Deionized Water (to make up 100%) 47.46

US PAT NO: 4,603,045 [IMAGE AVAILABLE] L4: 14 of 19
DATE ISSUED: Jul. 29, 1986
TITLE: Toothpaste for bonded (composite filling material) as well as natural teeth
INVENTOR: Irwin E. Smigel, 635 Madison Ave., New York, NY 10022
APPL-NO: 06/706,001
DATE FILED: Feb. 27, 1985
ART-UNIT: 123
PRIM-EXMR: Shep K. Rose
LEGAL-REP: Roberts, Spiecens & Cohen

US PAT NO: 4,603,045 [IMAGE AVAILABLE] L4: 14 of 19

ABSTRACT:
A toothpaste composition consisting essentially of, in percent by weight:
Dicalcium Phosphate, dihydrous: From 1.0% to 50%
Calcium Carbonate: From 1.0% to 50%
Sodium Bicarbonate: From 1.0% to 50%
Magnesium Carbonate: From 1.0% to 25%
Sorbitol 70%: From 1.0% to 50%
Corn Starch: From 0.5% to 10%
Cellulose Gum: From 0.5% to 5.0%
Calcium Peroxide: From 0.5% to 5%
Sodium Perborate: From 0.5% to 5%
Lathanol LAL (Sodium Lauryl Sulfoacetate): From 0.1% to 5%
Aluminum Hydroxide: From 0.01 to 1%
Saccharinate (Sodium Salt): From 0.05% to 2%
Flavoring material: From 0.05% to 2%
Alkylparaben: From 0.05% to 1.0%
Sodium Monofluoride Phosphate: From 0.70% to 0.80%
Titanium Dioxide: From 0.1% to 10%
Deinonized Water: From 10% to 50%.

SUMMARY:

BSUM(55)

. . .
0.7
Aluminum Hydroxide 0.1
Saccharinate (Sodium Salt) 0.5
Flavoring Material 1
Consisting of:
Menthol crystals 20%
0.1 of Spearment **NF** 20%
Terpeneless Spearmint 30%
Oil of Peppermint 20%
Oil of Anise (imitation) 10%
Methylparaben 0.5
(Hydroybenzoic acid methyl ester)
Propylparaben 0.03
(**Hydroxybenzoic** acid propylester)
Sodium Monofluoride Phosphate 0.76
Titanium Dioxide 1.0
Deinonized Water (to make up 100%) 47.46

US PAT NO: 4,323,694 [IMAGE AVAILABLE] L4: 15 of 19
DATE ISSUED: Apr. 6, 1982
TITLE: Benzoic acid esters
INVENTOR: Thomas L. Scala, Jr., West Milford, NJ
ASSIGNEE: Finetex, Inc., Elmwood Park, NJ (U.S. corp.)
APPL-NO: 06/258,801
DATE FILED: Apr. 29, 1981
ART-UNIT: 126
PRIM-EXMR: Paul J. Killos
LEGAL-REP: Weingram & Klauber

US PAT NO: 4,323,694 [IMAGE AVAILABLE] L4: 15 of 19

ABSTRACT:
The benzoic acid ester of an alcohol which is selected from the group consisting of (A) at least one C.sub.2n branched primary alcohol, wherein n is 5 through 9; (B) at least one C.sub.2m+1 branched or linear primary alcohol, wherein m is 4 through 9; and (C) mixtures comprising at least 40% and preferably at least 60% by weight of the members of (A) and (B), with one or more linear primary alcohols of even carbon number chain length. The benzoic acid esters are useful in skin care compositions, e.g., hand cleaners, bath oils, suntan oils, anti-perspirants, perfumes, colognes, cold creams, electric pre-shaves, eye and throat oils, topical pharmaceutical ointments, lipsticks, stick rouges, lotions, skin moisturizers, cleansing creams or after bath splashes or lotions.

DETDESC:

DETD(261)

. . .

% by wt.

A. Beeswax, white	11.00
Cetyl alcohol	2.50
Cetyl palmitate	2.20
Mineral oil, light, **NF**	28.00
Benzoate	20.60
Cerasynt Q (Glyceryl stearate, self-emulsifying).sup.1	0.75
Propyl paraben (propyl p-**hydroxybenzoate**)	0.05
B. Water, purified	32.83
Borax (sodium borate)	0.75
Methyl paraben (methyl p-**hydroxybenzoate**)	0.15
C. Water, purified	1.00
Dowicil 200 (Quaternium-15).sup.2	0.10
D. Fragrance	0.07

.sup.1 Van Dyk. . .

US PAT NO: 4,323,693 [IMAGE AVAILABLE] L4: 16 of 19
DATE ISSUED: Apr. 6, 1982
TITLE: Benzoic acid ester
INVENTOR: Thomas L. Scala, Jr., West Milford, NJ
ASSIGNEE: Finetex, Inc., Elmwood Park, NJ (U.S. corp.)
APPL-NO: 06/257,977
DATE FILED: Apr. 27, 1981
ART-UNIT: 126
PRIM-EXMR: Paul J. Killos
LEGAL-REP: Weingram & Klauber

US PAT NO: 4,323,693 [IMAGE AVAILABLE] L4: 16 of 19

ABSTRACT:
A substantially pure benzoic acid ester of isostearyl (C.sub.18) alcohol. The composition of this invention has unique properties in that it is non-greasy, has a low cloud point and pour point, is practically odorless, has low toxicity, and is stable. These properties make such composition useful as a vehicle or carrier, emollient or solubilizer for toiletry and cosmetic formulations, e.g., hair cream, hand cleaner, bath oil, suntan oil, brilliantine, anti-perspirants, perfumes and colognes, cold creams, electric pre-shave, eye and throat oil, fingernail polish, topical pharmaceutical ointments, lipsticks, stick rouge, skin lotions and creams, skin moisturizers, cleansing creams and after bath splash and lotions.

DETDESC:

DETD(220)

. . .

% by wt.

A. Beeswax, white	11.00
Cetyl alcohol	2.50
Cetyl palmitate	2.20
Mineral oil, light, **NF**	28.00
Isostearyl benzoate	20.60
Cerasynt Q (Glyceryl stearate, self-emulsifying).sup.1	0.75
Propyl paraben (propyl p-**hydroxybenzoate**)	0.05
B. Water, purified	32.83
Borax (sodium borate)	0.75
Methyl paraben (methyl p-**hydroxybenzoate**)	0.15
C. Water, purified	1.00
Dowicil 200 (Quaternium-15).sup.2	0.10
D. Fragrance	0.07

.sup.1 Van Dyk. . .

US PAT NO: 4,322,545 [IMAGE AVAILABLE] L4: 17 of 19
DATE ISSUED: Mar. 30, 1982
TITLE: Benzoic acid esters
INVENTOR: Thomas L. Scala, Jr., West Milford, NJ
ASSIGNEE: Finetex, Inc., Elmwood Park, NJ (U.S. corp.)
APPL-NO: 06/252,794
DATE FILED: Apr. 13, 1981
ART-UNIT: 126
PRIM-EXMR: Paul J. Killos
LEGAL-REP: Weingram & Klauber

US PAT NO: 4,322,545 [IMAGE AVAILABLE] L4: 17 of 19

ABSTRACT:
A substantially pure benzoic acid ester of a mixture of alcohols. The mixture of alcohols consists essentially of (A) at least one C.sub.12 or C.sub.14 primary alcohol and (B) at least one C.sub.13 or C.sub.15 primary alcohol. The weight ratio of the even carbon number alcohols (A) to the odd carbon number alcohols (B) is from about 0.25:1 to about 4:1, preferably from about 0.5:1 to about 3:1. At least 70% by weight of each alcohol is linear and substantially all of the remainder of each alcohol is branched at the two carbon position. The compositions of this invention have unique properties in that they are substantially non-greasy, lack oiliness and greasiness, have low cloud points and pour points, have a bland odor, low toxicity, and are stable. The properties make such compositions useful as a vehicle or carrier, emollient or solubilizer for toiletry and cosmetic formulations, e.g., hair cream, hand cleaner, bath oil, suntan oil, brilliantine, anti-perspirants, perfumes and colognes, cold creams, electric pre-shave, eye and throat oil, fingernail polish, topical pharmaceutical ointments, lipsticks, stick rouge, skin lotions and creams, skin moisturizers, cleansing creams and after bath splash and lotions.

DETDESC:

DETD(334)

. . .

% by wt.

A. Beeswax, white	11.00
Cetyl alcohol	2.50
Cetyl palmitate	2.20
Mineral oil, light, **NF**	28.00
NEODOL 25 benzoate	20.60
Cerasynt Q (Glyceryl stearate, self-emulsifying).sup.1	0.75
Propyl paraben (propyl p-**hydroxybenzoate**)	0.05
B. Water, purified	32.83
Borax (sodium borate)	0.75
Methyl paraben (methyl p-**hydroxybenzoate**)	0.15
C. Water, purified	1.00
Dowicil 200 (Quaternium-15).sup.2	0.10
D. Fragrance	0.07

.sup.1 Van Dyk. . .

US PAT NO: 4,306,076 [IMAGE AVAILABLE] L4: 18 of 19
DATE ISSUED: Dec. 15, 1981
TITLE: Inter-phenylene CBA compounds
INVENTOR: Norman A. Nelson, Galesburg, MI
ASSIGNEE: The Upjohn Company, Kalamazoo, MI (U.S. corp.)
APPL-NO: 06/219,131
DATE FILED: Dec. 22, 1980
ART-UNIT: 126
PRIM-EXMR: Paul J. Killos
LEGAL-REP: L. Ruth Hattan, Robert A. Armitage

US PAT NO: 4,306,076 [IMAGE AVAILABLE] L4: 18 of 19

ABSTRACT:
The present specification provides novel analogs of carbacyclin (CBA.sub.2), 6a-carba-prostacyclin (6a-carba-PGI.sub.2), which have pronounced prostacyclin-like pharmacological activity, e.g., as platelet anti-aggregatory agents. Specifically the novel chemical analogs of CBA.sub.2 are those substituted by fluoro (C-5), alkyl (C-9), interphenylene (C-5), and methano (C-6a,9). Further provided are benzindene analogs of CBA.sub.2 and substituted forms thereof, i.e., 9-deoxy-2',9-methano (or 2',9-metheno)-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)-PGF.sub.1 compounds. Also provided are a variety of novel chemical intermediates, e.g., substituted bicyclo[3.3.0]octane intermediates, and chemical process utilizing such intermediates which are useful in the preparation of the novel CBA.sub.2 analogs.

SUMMARY:

BSUM(132)

(1) . . . N-methyl-N-cyclohexylamide, N-ethyl-N-cyclopentylamide, and N-ethyl-Ncyclohexylamide. Amides within the scope of aralkylamino are benzylamide, 2-phenylethylamide, and N-methyl-N benzyl-amide. Amides within the scope **nf** substituted phenylamide are p-chloroanilide, m-chloroanilide, 2,4-dichloroanilide, 2,4,6-trichloroanilide, m-nitroanilide, p-nitroanilide, p-methoxyanilide, 3,4-dimethoxyanilide, 3,4,5-trimethoxyanilide, p-hydroxymethylanilide, p-methylanilide, m-methyl anilide, p-ethylanilide, t-butylanilide, p-carboxyanilide,

p-methoxycarbonyl. . . benzoylalkylamino are p-chlorobenzoylmethylamide, m-chlorobenzoylmethylamide, 2,4-dichlorobenzoylmethylamide, 2,4,6-trichlorobenzoylmethylamide, m-nitrobenzoylmethylamide, p-nitrobenzoylmethylamide, p-methoxybenzoylmethylamide, 2,4-dimethoxy benzoylmethylamide, 3,4,5-trimethoxybenzoylmethylamide, p-hydroxymethylbenzoylmethylamide, p-methylbenzoylmethylamide, m-methylbenzoylmethylamide, p-ethylbenzoylmethylamide, t-butylbenzoylmethylamide, p-carboxybenzoylmethylamide, m-methoxycarbonylbenzoylmethylamide, o-carboxybenzoylmethylamide, o-**hydroxybenzoylmethylamide**, p-chlorobenzoylethylamide, m-chlorobenzoylethylamide, 2,4-dichlorobenzoylethylamide, 2,4,6-trichlorobenzoylethylamide, m-nitrobenzoylethylamide, p-nitrobenzoylethylamide, p-methoxybenzoylethylamide, p-methoxybenzoylethylamide, 2,4-dimethoxybenzoylethylamide, 3,4,5trimethoxybenzoylethylamide, p-hydroxymethylbenzoylethylamide, p-methylbenzoylethylamide, m-methylbenzoylethylamide, p-ethylbenzoylethylamide, t-butylbenzoylethylamide, p-carboxybenzoylethylamide, m-methoxycarbonylbenzoylethylamide, o-carboxybenzoylethylamide, o-**hydroxybenzoylethylamide**, p-chlorobenzoylpropylamide, m-chlorobenzoylpropylamide, 2,4-dichlorobenzoylpropylamide, 2,4,6-trichlorobenzoylpropylamide, m-nitrobenzoylpropylamide, p-nitrobenzoylpropylamide, p-methoxybenzoylpropylamide, 2,4-dimethoxybenzoylpropylamide, 3,4,5-trimethoxybenzoylpropylamide, p-hydroxymethylbenzoylpropylamide, p-methylbenzoylpropylamide, m-methylbenzoylpropylamide, p-ethylbenzoylpropylamide, t-butylbenzoylpropylamide, p-carboxybenzoylpropylamide, m-methoxycarbonylbenzoylpropylamide, o-carboxybenzoylpropylamide, o-**hydroxybenzoylpropylamide**, p-chlorobenzoylbutylamide, m-chlorobenzoylbutylamide, 2,4-dichlorobenzoylbutylamide, 2,4,6-trichlorobenzoylbutylamide, m-nitrobenzoylmethylamide, p-nitrobenzoylbutylamide, p-methoxybenzoylbutylamine, 2,4-dimethoxybenzoylbutyl-amide, 3,4,5-trimethoxybenzoylbutylamide, p-hydroxymethylbenzoylbutyl-amide, p-methylbenzoylbutyamide, m-methylbenzoylbutylamide, p-ethyl-benzoylbutylamide, m-methylbenzoylbutylamide, p-ethylbenzoylbutyl-amide, t-butylbenzoylbutylamide, p-carboxybenzoylbutylamide, m-methoxycarbonylbenzoylbutylamide, o-carboxybenzoylbutylamide, o-**hydroxybenzoylmethylamide**. Amides within the scope of pyridylamino are .alpha.-pyridylamide, .beta.-pyridylamide, and .gamma.-pyridylamide. Amides within the scope of substituted pyridylamino are 4-methyl-.alpha.-pyridylamide,. . .

US PAT NO: 4,306,075 [IMAGE AVAILABLE] L4: 19 of 19
DATE ISSUED: Dec. 15, 1981
TITLE: Composition and process
INVENTOR: Paul A. Aristoff, Portage, MI
ASSIGNEE: The Upjohn Company, Kalamazoo, MI (U.S. corp.)
APPL-NO: 06/219,210
DATE FILED: Dec. 22, 1980
ART-UNIT: 126
PRIM-EXMR: PauL J. Killos
LEGAL-REP: L. Ruth Hattan, Robert A. Armitage

US PAT NO: 4,306,075 [IMAGE AVAILABLE] L4: 19 of 19

ABSTRACT:
The present specification provides novel analogs of carbacyclin (CBA.sub.2), 6a-carba-prostacyclin (6a-carba-PGI.sub.2), which have pronounced prostacyclin-like pharmacological activity, e.g., as platelet antiaggregatory agents. Specifically the novel chemical analogs of CBA.sub.2 are those substituted by fluoro (C-5), alkyl (C-9), interphenylene (C-5), and methano (C-6a,9). Further provided are benzindene analogs of CBA.sub.2 and substituted forms thereof, i.e., 9-deoxy-2',9-methano (or 2',9-metheno)-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)-PGF.sub.1 compounds. Also provided are a variety of novel chemical intermediates, e.g., substituted bicyclo[3.3.0]octane intermediates, and chemical process utilizing such intermediates which are useful in the preparation of the novel CBA.sub.2 analogs.

SUMMARY:

BSUM(132)

(1) . . . N-methyl-N-cyclohexylamide, N-ethyl-N-cyclopentylamide, and N-ethyl-Ncyclohexylamide. Amides within the scope of aralkylamino are benzylamide, 2-phenylethylamide, and N-methyl-N benzyl-amide. Amides within the scope **nf** substituted phenylamide are p-chloroanilide, m-chloroanilide, 2,4-dichloroanilide, 2,4,6-trichloroanilide, m-nitroanilide, p-nitroanilide, p-methoxyanilide, 3,4-dimethoxyanilide, 3,4,5-trimethoxyanilide, p-hydroxymethylanilide, p-methylanilide, m-methyl anilide, p-ethylanilide, t-butylanilide, p-carboxyanilide, p-methoxycarbonyl. . . benzoylalkylamino are p-chlorobenzoylmethylamide, m-chlorobenzoylmethylamide, 2,4-dichlorobenzoylmethylamide, 2,4,6-trichlorobenzoylmethylamide, m-nitrobenzoylmethylamide, p-nitrobenzoylmethylamide, p-methoxybenzoylmethylamide, 2,4-dimethoxy benzoylmethylamide, 3,4,5-trimethoxybenzoylmethylamide, p-hydroxymethylbenzoylmethylamide, p-methylbenzoylmethylamide, m-methylbenzoylmethylamide, p-ethylbenzoylmethylamide, t-butylbenzoylmethylamide, p-carboxybenzoylmethylamide, m-methoxycarbonylbenzoylmethylamide, o-carboxybenzoylmethylamide, o-**hydroxybenzoylmethylamide**, p-chlorobenzoylethylamide, m-chlorobenzoylethylamide, 2,4-dichlorobenzoylethylamide, 2,4,6-trichlorobenzoylethylamide, m-nitrobenzoylethylamide, p-nitrobenzoylethylamide, p-methoxybenzoylethylamide, p-methoxybenzoylethylamide, 2,4-dimethoxybenzoylethylamide, 3,4,5trimethoxybenzoylethylamide, p-hydroxymethylbenzoylethylamide, p-methylbenzoylethylamide, m-methylbenzoylethylamide, p-ethylbenzoylethylamide, t-butylbenzoylethylamide, p-carboxybenzoylethylamide, m-methoxycarbonylbenzoylethylamide, o-carboxybenzoylethylamide, o-**hydroxybenzoylethylamide**, p-chlorobenzoylpropylamide, m-chlorobenzoylpropylamide, 2,4-dichlorobenzoylpropylamide, 2,4,6-trichlorobenzoylpropylamide, m-nitrobenzoylpropylamide, p-nitrobenzoylpropylamide, p-methoxybenzoylpropylamide, 2,4-dimethoxybenzoylpropylamide, 3,4,5-trimethoxybenzoylpropylamide, p-hydroxymethylbenzoylpropylamide, m-methylbenzoylpropylamide, p-ethylbenzoylpropylamide, t-butylbenzoylpropylamide, p-carboxybenzoylpropylamide, m-methoxycarbonylbenzoylpropylamide, o-carboxybenzoylpropylamide, o-**hydroxybenzoylpropylamide**, p-chlorobenzoylbutylamide, m-chlorobenzoylbutylamide, 2,4-dichlorobenzoylbutylamide, 2,4,6-trichlorobenzoylbutylamide, m-nitrobenzoylmethylamide, p-nitrobenzoylbutylamide, p-methoxybenzoylbutylamine, 2,4-dimethoxybenzoylbutyl-amide, 3,4,5-trimethoxybenzoylbutylamide, p-hydroxymethylbenzoylbutyl-amide, p-methylbenzoylbutyamide, m-methylbenzoylbutylamide, p-ethyl-benzoylbutylamide, m-methylbenzoylbutylamide, p-ethylbenzoylbutyl-amide, t-butylbenzoylbutylamide, p-carboxybenzoylbutylamide, m-methoxycarbonylbenzoylbutylamide, o-carboxybenzoylbutylamide, o-**hydroxybenzoylmethylamide**. Amides within the scope of pyridylamino are .alpha.-pyridylamide, .beta.-pyridylamide, and .gamma.-pyridylamide. Amides within the scope of substituted pyridylamino are 4-methyl-.alpha.-pyridylamide,. . .

=> s ((nuclear factor) (3a) (b or K or kappa)) or (nfkb) or (nf kb)

62536 NUCLEAR
268223 FACTOR
205 NUCLEAR FACTOR
(NUCLEAR(W)FACTOR)
1219215 B
374077 K
4991 KAPPA
59 (NUCLEAR FACTOR) (3A) (B OR K OR KAPPA)
51 NFKB
11097 NF
16285 KB
118 NF KB
(NF(W)KB)
L5 198 ((NUCLEAR FACTOR) (3A) (B OR K OR KAPPA)) OR (NFKB) OR (NF KB)

=> s l2 (p) l5

L6 0 L2 (P) L5

=> s l2 and l5

L7 10 L2 AND L5

=> s l1 and l7

L8 0 L1 AND L7

=> d l7 1-10 bib rel ab

US PAT NO: 5,885,829 [IMAGE AVAILABLE] L7: 1 of 10
DATE ISSUED: Mar. 23, 1999
TITLE: Engineering oral tissues
INVENTOR: David J. Mooney, Ann Arbor, MI
Robert B. Rutherford, Ann Arbor, MI
ASSIGNEE: The Regents of the University of Michigan, Ann Arbor, MI (U.S. corp.)
APPL-NO: 08/864,494
DATE FILED: May 28, 1997
ART-UNIT: 191
PRIM-EXMR: Nancy Degen
LEGAL-REP: Arnold, White & Durkee

US PAT NO: 5,885,829 [IMAGE AVAILABLE] L7: 1 of 10

ABSTRACT:
Disclosed are methods for regenerating dental and oral tissues from viable cells using ex vivo culture on a structural matrix. The regenerated oral tissues and tissue-matrix preparations thus provided have both clinical applications in dentistry and oral medicine and are

also useful in in vitro toxicity and biocompatibility testing.

US PAT NO: 5,874,448 [IMAGE AVAILABLE] L7: 2 of 10
DATE ISSUED: Feb. 23, 1999
TITLE: Substituted 2-(2,6 dioxo-3-fluoropiperidin-3-yl)-isoindolines and method of reducing TNF.alpha. levels
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger Shen-Chu Chen, Edison, NJ
Hon-Wah Man, Neshanic Station, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/976,140
DATE FILED: Nov. 18, 1997
ART-UNIT: 162
PRIM-EXMR: Evelyn Huang
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,874,448 [IMAGE AVAILABLE] L7: 2 of 10

ABSTRACT:
1-Oxo-2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindolines and 1,3-dioxo-2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindolines reduce the levels of TNF.alpha. in a mammal. A typical embodiment is 1,3-dioxo-2-(2,6-dioxo-3-fluoropiperidin-3-yl)-isoindoline.

US PAT NO: 5,849,263 [IMAGE AVAILABLE] L7: 3 of 10
DATE ISSUED: Dec. 15, 1998
TITLE: Pharmaceutical compositions containing alkylaryl polyether alcohol polymer
INVENTOR: Thomas P. Kennedy, Richmond, VA
ASSIGNEE: Charlotte-Mecklenburg Hospital Authority, Charlotte, NC (U.S. corp.)
APPL-NO: 08/638,893
DATE FILED: Apr. 25, 1996
ART-UNIT: 166
PRIM-EXMR: Robert H. Harrison
LEGAL-REP: Bell Seltzer Intellectual Property Law Group of Alston & Bird LLP

US PAT NO: 5,849,263 [IMAGE AVAILABLE] L7: 3 of 10
REL-US-DATA: Continuation-in-part of Ser. No. 299,316, Aug. 31, 1994, Pat. No. 5,512,270, which is a continuation-in-part of Ser. No. 39,732, Mar. 30, 1993, abandoned.

ABSTRACT:
There is provided novel pharmaceutical compositions containing tyloxapol as the active ingredient. These formulations comprise tyloxapol at concentrations above 0.125%, preferably from about 0.25% to about 5.0%. In addition, the invention encompasses pharmaceutical compositions having reduced hypertonicity which compositions comprise tyloxapol in pharmaceutically acceptable solutions without significant concentrations of hypertonic agents or other active ingredients NaHCO.sub.3, or active phospholipids, such as DPPC. The less hypertonic formulations allow one to derive all the benefits of the active ingredient tyloxapol, such as its reduced toxicity and enhanced half-life, while avoiding or reducing side effects, such as bronchospasms, associated with the various hypertonic agents or other active ingredient agents.

US PAT NO: 5,840,277 [IMAGE AVAILABLE] L7: 4 of 10
DATE ISSUED: Nov. 24, 1998
TITLE: Treatment of chronic pulmonary inflammation
INVENTOR: Andrew J. Ghio, Durham, NC
Thomas P. Kennedy, Richmond, VA
ASSIGNEE: Charlotte Hospital Authority, Charlotte, NC (U.S. corp.)
APPL-NO: 08/632,275
DATE FILED: Apr. 15, 1996
ART-UNIT: 185
PRIM-EXMR: David Guzo
LEGAL-REP: The Bell Seltzer Intellectual Law Firm of Alston & Bird, LLP

US PAT NO: 5,840,277 [IMAGE AVAILABLE] L7: 4 of 10
REL-US-DATA: Continuation-in-part of Ser. No. 413,699, Mar. 30, 1995, which is a continuation-in-part of Ser. No. 219,770, Mar. 29, 1994, Pat. No. 5,474,760, Dec. 12, 1995, which is a continuation-in-part of Ser. No. 299,316, Aug. 31, 1994, Pat. No. 5,512,270, which is a continuation-in-part of Ser. No. 39,732, Mar. 30, 1993, abandoned.

ABSTRACT:
A method and medicant for the inhibition of activation of the nuclear transcription NF-.kappa.B comprising administering an effective amount of a compound of the formula: ##STR1## where R=ethylene, R'=C.sub.4 to C.sub.14 straight chain or branched alkyl, x is greater than 1, and y=8 to 18 is provided. The medicant is preferably administered by aerosolization into the mammalian respiratory system. The medicant may also be applied to the mammalian skin. Preferably the medicant includes a physiologically acceptable carrier which may be selected from buffered saline, isotonic saline, normal saline, petroleum-based ointments and U.S.P. cold cream. There is further provided a method wherein said medicant includes an anti-inflammatory steroid. In addition a method and medicant for treating cutaneous inflammatory disorders, inhibiting the secretion of the pro-inflammatory cytokines TNF, IL-1, IL-6, IL-8 and the growth factor GM-CSF is provided.

US PAT NO: 5,798,368 [IMAGE AVAILABLE] L7: 5 of 10
DATE ISSUED: Aug. 25, 1998
TITLE: Tetrasubstituted 2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolines and method of reducing TNF.alpha. levels
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger Shen-Chu Chen, Edison, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/701,494
DATE FILED: Aug. 22, 1996
ART-UNIT: 164
PRIM-EXMR: James H. Reamer
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,798,368 [IMAGE AVAILABLE] L7: 5 of 10

ABSTRACT:
Tetrasubstituted 1-oxo-2-(2,6-dioxopiperidin-3-yl)isoindolines reduce the levels of TNF.alpha. in a mammal. A typical embodiment is 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4,5,6,7-tetrafluoroisoindoline.

US PAT NO: 5,670,617 [IMAGE AVAILABLE] L7: 6 of 10
DATE ISSUED: Sep. 23, 1997
TITLE: Nucleic acid conjugates of tat-derived transport polypeptides
INVENTOR: Alan Frankel, 21 Marinero Cir. #206, Tiburon, CA 94920
Carl Pabo, 18 Weldon Rd., Newton, MA 02158
James G. Barsoum, 9 Marlboro Rd., Lexington, MA 02173
Stephen E. Fawell, One Black Horse Ter., Winchester, MA 01890
R. Blake Pepinsky, 30 Falmouth Rd., Arlington, MA 02174
APPL-NO: 08/450,246
DATE FILED: May 25, 1995
ART-UNIT: 189
PRIM-EXMR: George C. Elliot
ASST-EXMR: Thomas G. Larson
LEGAL-REP: James F. Haley, Jr., Madge R. Kanter

US PAT NO: 5,670,617 [IMAGE AVAILABLE] L7: 6 of 10
REL-US-DATA: Division of Ser. No. 235,403, Apr. 28, 1994, which is a continuation-in-part of Ser. No. 158,015, Nov. 24, 1993, abandoned, which is a continuation of Ser. No. 636,662, Jan. 2, 1991, abandoned, which is a continuation-in-part of Ser. No. 454,450, Dec. 21, 1989, abandoned, said Ser. No. 235,403 is a continuation-in-part of Ser. No. 934,375, Aug. 21, 1992, abandoned.

ABSTRACT:
This invention relates to delivery of biologically active cargo molecules, such as polypeptides and nucleic acids, into the cytoplasm and nuclei of cells in vitro and in vivo. Intracellular delivery of cargo molecules according to this invention is accomplished by the use of novel transport polypeptides which comprise HIV tat protein or one or more portions thereof, and which are covalently attached to cargo molecules. The transport polypeptides in preferred embodiments of this invention are characterized by the presence of the tat basic region (amino acids 49-57), the absence of the tat cysteine-rich region (amino acids 22-36) and the absence of the tat exon 2-encoded carboxy-terminal domain (amino acids 73-86) of the naturally-occurring tat protein. By virtue of the absence of the cysteine-rich region, the preferred transport polypeptides of this invention solve the potential problems of spurious trans-activation and disulfide aggregation. The reduced size of the preferred transport polypeptides of this invention also minimizes interference with the biological activity of the cargo molecule.

US PAT NO: 5,635,517 [IMAGE AVAILABLE] L7: 7 of 10
DATE ISSUED: Jun. 3, 1997
TITLE: Method of reducing TNF.alpha. levels with amino substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxo-and 1,3-dioxoisoindolines
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger S. -C. Chen, Edison, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/690,258
DATE FILED: Jul. 24, 1996
ART-UNIT: 123
PRIM-EXMR: C. Warren Ivy

ASST-EXMR: C. S. Aulakh
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,635,517 [IMAGE AVAILABLE] L7: 7 of 10

ABSTRACT:
1-Oxo- and 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl) isoindolines substituted with amino in the benzo ring reduce the levels of TNF.alpha. in a mammal. A typical embodiment is 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)-5-aminoisoindoline.

US PAT NO: 5,612,330 [IMAGE AVAILABLE] L7: 8 of 10
DATE ISSUED: Mar. 18, 1997
TITLE: Methods for inhibiting and controlling viral growth
INVENTOR: David T. Connor, Ann Arbor, MI
Stephen J. Gracheck, Ann Arbor, MI
ASSIGNEE: Warner-Lambert Company, Morris Plains, NJ (U.S. corp.)
APPL-NO: 08/408,431
DATE FILED: Mar. 22, 1995
ART-UNIT: 122
PRIM-EXMR: Robert T. Bond
LEGAL-REP: Charles W. Ashbrook

US PAT NO: 5,612,330 [IMAGE AVAILABLE] L7: 8 of 10
REL-US-DATA: Continuation-in-part of Ser. No. 351,611, Dec. 12, 1994, Pat. No. 5,489,586, which is a continuation-in-part of Ser. No. 207,330, Mar. 7, 1994, abandoned.

ABSTRACT:
Benzothiophene, benzofuran and indolethiazepinones, oxazepinones, and diazepinones are effective therapeutic agents for treating viral diseases, including those caused by herpesvirus and HIV.

US PAT NO: 5,608,095 [IMAGE AVAILABLE] L7: 9 of 10
DATE ISSUED: Mar. 4, 1997
TITLE: Alkyl-4-silyl-phenols and esters thereof as antiatherosclerotic agents
INVENTOR: Roger A. Parker, Cincinnati, OH
Michael L. Edwards, Cincinnati, OH
Mark J. Vaal, Cincinnati, OH
James E. Matt, Jr., Cincinnati, OH
Kim S. Chen, Cincinnati, OH
Mark T. Yates, Ann Arbor, MI
Paul S. Wright, Cincinnati, OH
Steven J. Busch, West Chester, OH
ASSIGNEE: Hoechst Marion Roussel, Inc., Cincinnati, OH (U.S. corp.)
APPL-NO: 08/637,968
DATE FILED: Apr. 30, 1996
ART-UNIT: 124
PRIM-EXMR: Paul F. Shaver
LEGAL-REP: William R. Boudreaux

US PAT NO: 5,608,095 [IMAGE AVAILABLE] L7: 9 of 10

ABSTRACT:
This invention relates to compounds of the formula ##STR1## wherein R.sub.1 and R.sub.6 are each independently C.sub.1 -C.sub.6 alkyl; R.sub.2, R.sub.3 and R.sub.4 are each independently hydrogen or C.sub.1 -C.sub.6 alkyl; R is hydrogen or --C(O)--(CH.sub.2).sub.m --Q wherein Q is hydrogen or --COOH and m is an integer 1, 2, 3 or 4; Z is a thio, oxy or methylene group; A is a C.sub.1 -C.sub.4 alkylene group; R.sub.5 and R.sub.7 are each independently a C.sub.1 -C.sub.6 alkyl or --(CH.sub.2).sub.n --(Ar) wherein n is an integer 0, 1, 2 or 3; and Ar is phenyl or naphthyl unsubstituted or substituted with one to three substituents selected from the group consisting of hydroxy, methoxy, ethoxy, halogen, trifluoromethyl, C.sub.1 -C.sub.6 alkyl, or --NR.sub.8 R.sub.9, wherein R.sub.8 and R.sub.9 are each independently hydrogen or C.sub.1 -C.sub.6 alkyl; with the proviso that when R.sub.2 and at least one of R.sub.5 or R.sub.7 is C.sub.1 -C.sub.6 alkyl, and Ar is not substituted with trifluoromethyl or --NR.sub.8 R.sub.9, then R is --C(O)--(CH.sub.2).sub.m --Q; or a pharmaceutically acceptable salt thereof; useful for the treatment of atherosclerosis and chronic inflammatory disorders; for inhibiting cytokine-induced expression of VCAM-1 and/or ICAM-1; for inhibiting the peroxidation of LDL lipid; for lowering plasma cholesterol; and as antioxidant chemical additives useful for preventing oxidative deterioration in organic materials.

US PAT NO: 5,317,019 [IMAGE AVAILABLE] L7: 10 of 10
DATE ISSUED: May 31, 1994
TITLE: Inhibition of interleukin-1 and tumor necrosis factor production by monocytes and/or macrophages
INVENTOR: Paul E. Bender, Cherry Hill, NJ
Don E. Griswold, North Wales, PA
Nabil Hanna, Solana Beach, CA
John C. Lee, Radnor, PA
Bartholomew J. Votta, Pottstown, PA
Philip L. Simon, Randolph, NJ
Alison M. Badger, Bryn Mawr, PA
Klaus M. Esser, Downingtown, PA
ASSIGNEE: SmithKline Beecham Corp., Phildelphia, PA (U.S. corp.)
APPL-NO: 07/809,484
DATE FILED: Dec. 12, 1991
ART-UNIT: 123
PRIM-EXMR: C. Warren Ivy
ASST-EXMR: Raymond Covington
LEGAL-REP: Dara L. Dinner, Stephen Venetianer, Edward T. Lentz

US PAT NO: 5,317,019 [IMAGE AVAILABLE] L7: 10 of 10
REL-US-DATA: Continuation-in-part of Ser. No. 365,349, Jun. 13, 1989, abandoned.

ABSTRACT:

A method of inhibiting the production of interleukin-1 by monocytes and/or macrophages in a human in need thereof which comprises administering to such a human an effective, interleukin-1 production inhibiting amount of a diaryl-substituted imidazole fused to a second heterocyclic ring containing a nitrogen bridgehead atom wherein said second ring may also contain sulfur, oxygen or an additional nitrogen atom, and may contain additional unsaturation.
This invention relates to a method of inhibiting the production of Tumor Necrosis Factor (TNF) by monocytes or macrophages in a human in need thereof which comprises administering to such mammal an effective, TNF production inhibiting amount of a compound of Formula (I) as described herein. The compounds of Formula (II) are generally described as diaryl-substituted imidazole fused to a second heterocyclic ring containing a nitrogen bridgehead wherein said ring may also contain sulfur, oxygen, or an additional nitrogen atom, and may contain additional unsaturation.

=> s (l2 or l5) (p) (treat? or therap? or medic? or pharmac? or drug#)

586240 TREAT?
89576 THERAP?
142287 MEDIC?
116190 PHARMAC?
73018 DRUG#
L9 6200 (L2 OR L5) (P) (TREAT? OR THERAP? OR MEDIC? OR PHARMAC? OR DRUG#)

=> s l9 and 514/clas

80898 514/CLAS
L10 3942 L9 AND 514/CLAS

=> s l9 and 564/clas

32158 564/CLAS
L11 471 L9 AND 564/CLAS

=> s l10 and l11

L12 288 L10 AND L11

=> s l5 and 514/clas

80898 514/CLAS
L13 72 L5 AND 514/CLAS

=> s l5 and 564/clas

32158 564/CLAS
L14 6 L5 AND 564/CLAS

=> s l13 or l14

L15 72 L13 OR L14

=> d 1-72 bib kwic

US PAT NO: 5,905,089 [IMAGE AVAILABLE] L15: 1 of 72
DATE ISSUED: May 18, 1999
TITLE: Use of sesquiterpene lactones for treatment of severe inflammatory disorders
INVENTOR: Daniel H. Hwang, Baton Rouge, LA
Nikolaus H. Fischer, Baton Rouge, LA
ASSIGNEE: Board of Supervisors of Louisiana State University and Agricultural and Mechanical College, Baton Rouge, LA (U.S. corp.)
APPL-NO: 09/059,480
DATE FILED: Apr. 13, 1998
ART-UNIT: 164
PRIM-EXMR: Keith D. MacMillan

LEGAL-REP: Bonnie J. Davis, John H. Runnels

US PAT NO: 5,905,089 [IMAGE AVAILABLE] L15: 1 of 72
US-CL-CURRENT: **514/468**

DETDESC:

DETD(60)

Parthenolide inhibits Nuclear Factor--kB (**NF**-**kB**) transcription factor that has been activated by LPS in the murine macrophage cell line (RAW 264.7) as assessed by the degradation of the protein, IKB.sub..alpha.. Activated **NF**-**kB** is known to induce the expression of many early response genes including inducible nitric oxide synthetase, cyclooxygenase, and chemokines that. . .

US PAT NO: 5,900,430 [IMAGE AVAILABLE] L15: 2 of 72
DATE ISSUED: May 4, 1999
TITLE: Cytokine inhibitors
INVENTOR: Alison Mary Badger, Bryn Mawr, PA
Wanda Bernadette High, Wayne, PA
ASSIGNEE: AnorMED, Inc., Langley, Canada (foreign corp.)
APPL-NO: 08/779,418
DATE FILED: Jan. 7, 1997
ART-UNIT: 125
PRIM-EXMR: Jerome D. Goldberg
LEGAL-REP: Kate H.Morrison & Foerster, LLP Murashige

US PAT NO: 5,900,430 [IMAGE AVAILABLE] L15: 2 of 72
US-CL-CURRENT: **514/409**, **212**, **278**

DETDESC:

DETD(29)

Osborn . . . molecular mechanism for the virus inducing activity of TNF is due to TNF's ability to activate a gene regulatory protein (**NF**-**kB**) found in the cytoplasm of cells, which promotes HIV replication through binding to a viral regulatory gene sequence (LTR).

US PAT NO: 5,883,081 [IMAGE AVAILABLE] L15: 3 of 72
DATE ISSUED: Mar. 16, 1999
TITLE: Isolation of novel HIV-2 proviruses
INVENTOR: Gunter Kraus, La Jolla, CA
Flossie Wong-Staal, San Diego, CA
Randy Talbott, Princeton, NJ
Eric M. Poeschla, San Diego, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/659,251
DATE FILED: Jun. 7, 1996
ART-UNIT: 168
PRIM-EXMR: Jeffrey Stucker
ASST-EXMR: Hankyel Park
LEGAL-REP: Townsend and Townsend and Crew

US PAT NO: 5,883,081 [IMAGE AVAILABLE] L15: 3 of 72
US-CL-CURRENT: **514/44**; 424/160.1; 435/69.1, 320.1; 530/388.35; 536/23.1

DETDESC:

DETD(215)

Several . . . before the SpI binding sites. This deletion is not seen in other HIV-2 isolates, and is not similar to the **NFkB** duplication (Novembre, et al. (1991) Journal of Medical Primatology 20, 188-92) previously described in the SIV.sub.MMpbj LTR.

US PAT NO: 5,877,203 [IMAGE AVAILABLE] L15: 4 of 72
DATE ISSUED: Mar. 2, 1999
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/722,438
DATE FILED: Oct. 17, 1996
ART-UNIT: 163
PRIM-EXMR: Deborah C. Lambkin
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,877,203 [IMAGE AVAILABLE] L15: 4 of 72
US-CL-CURRENT: **514/423**, **212**, **330**, **551**, **599**, **707**, **712**

DETDESC:

DETD(28)

At the molecular level, PDTC has been shown to inhibit the activation of the transcriptional regulatory factor **Nf**-**kB** in response to certain cytokine and non-cytokine stimuli (Schreck, Rieber et al. 1991; Schreck, Meier et al. 1992). However, by. . . has been discovered that endothelial cells activate VCAM-1 gene expression through an apparently novel transcriptional regulatory factor that is not **Nf**-**kB**. This suggests that PDTC may regulate endothelial cell gene expression through its effect on a new transcriptional regulatory protein. It. . .

US PAT NO: 5,877,200 [IMAGE AVAILABLE] L15: 5 of 72
DATE ISSUED: Mar. 2, 1999
TITLE: Cyclic amides
INVENTOR: George W. Muller, Bridgewater, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/920,715
DATE FILED: Aug. 29, 1997
ART-UNIT: 162
PRIM-EXMR: John Kight
ASST-EXMR: D. Margaret M. Mach
LEGAL-REP: Mathews, Collins Shepherd & Gould, P.A.

US PAT NO: 5,877,200 [IMAGE AVAILABLE] L15: 5 of 72
US-CL-CURRENT: **514/411**; 548/450, 451

SUMMARY:

BSUM(13)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,874,448 [IMAGE AVAILABLE] L15: 6 of 72
DATE ISSUED: Feb. 23, 1999
TITLE: Substituted 2-(2,6 dioxo-3-fluoropiperidin-3-yl)-isoindolines and method of reducing TNF.alpha. levels
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger Shen-Chu Chen, Edison, NJ
Hon-Wah Man, Neshanic Station, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/976,140
DATE FILED: Nov. 18, 1997
ART-UNIT: 162
PRIM-EXMR: Evelyn Huang
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,874,448 [IMAGE AVAILABLE] L15: 6 of 72
US-CL-CURRENT: **514/323**; 546/201

SUMMARY:

BSUM(13)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al., Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,869,055 [IMAGE AVAILABLE] L15: 7 of 72
DATE ISSUED: Feb. 9, 1999
TITLE: Anti-inflammatory CD14 polypeptides
INVENTOR: Shao-Chieh Juan, Moorpark, CA
Henri S. Lichenstein, Boulder, CO
Samuel D. Wright, Westfield, NJ
ASSIGNEE: Amgen, Inc., Thousand Oaks, CA (U.S. corp.)
APPL-NO: 08/484,397
DATE FILED: Jun. 7, 1995
ART-UNIT: 186
PRIM-EXMR: Thomas M. Cunningham
ASST-EXMR: Martha T. Lubet
LEGAL-REP: Timothy J. Gaul, Ron K. Levy, Steven M. Odre

US PAT NO: 5,869,055 [IMAGE AVAILABLE] L15: 7 of 72
US-CL-CURRENT: 424/185.1; **514/2**; 530/300, 317, 351; 536/23.5

DETDESC:

DETD(93)

LPS . . . eliminated formation of both complexes (data not shown). Stimulation of U373 cells with sCD14.sub.(7-10)A and LPS caused only 5%

of **NF**-**kB** activation as quantitated by gel scanning (FIG. 6, lane 6). Comparatively, stimulation of U373 cells with a mutant which does. .

US PAT NO: 5,863,904 [IMAGE AVAILABLE] L15: 8 of 72
DATE ISSUED: Jan. 26, 1999
TITLE: Methods for treating cancers and restenosis with P21
INVENTOR: Gary J. Nabel, Ann Arbor, MI
Zhi-yong Yang, Ann Arbor, MI
Elizabeth G. Nabel, Ann Arbor, MI
ASSIGNEE: The University of Michigan, Ann Arbor, MI (U.S. corp.)
APPL-NO: 08/533,942
DATE FILED: Sep. 26, 1995
ART-UNIT: 189
PRIM-EXMR: Jasemine C. Chambers
ASST-EXMR: Karen M. Hauda
LEGAL-REP: Brinks Hofer Gilson & Lione

US PAT NO: 5,863,904 [IMAGE AVAILABLE] L15: 8 of 72
US-CL-CURRENT: **514/44**; 435/69.1, 375

SUMMARY:

BSUM(13)

The . . . as well as the induction of the differentiated phenotype arises from altered patterns of gene expression, mediated in part by **NF**-**kB**, resulting from p21 induced transcriptional regulation leading to terminal differentiation and growth arrest. Previous attempts to induce antitumor effects through. . .

US PAT NO: 5,861,290 [IMAGE AVAILABLE] L15: 9 of 72
DATE ISSUED: Jan. 19, 1999
TITLE: Methods and polynucleotide constructs for treating host cells for infection or hyperproliferative disorders
INVENTOR: Mark A. Goldsmith, 20 Maple St., West Roxbury, MA 02132
Robert O. Ralston, 2863 Judah, San Francisco, CA 94122
APPL-NO: 07/965,039
DATE FILED: Oct. 22, 1992
ART-UNIT: 185
PRIM-EXMR: Jonny F. Railey, II
LEGAL-REP: Norman J. Kruse, Donald J. Pochopien, Robert P. Blackburn

US PAT NO: 5,861,290 [IMAGE AVAILABLE] L15: 9 of 72
US-CL-CURRENT: 424/93.2; 435/320.1; **514/44**; 536/23.1, 23.2, 23.5, 23.53, 23.6, 23.7, 23.72, 24.1, 24.5

DETDESC:

DETD(6)

The . . . contains both the tar region, which is highly selective for HIV tat, and also a region activated by the endogenous **nuclear** **factor** NF-.**kappa**.**B** (the LTR has tandem NF-.kappa.B binding regions). Although the tar sequence strongly suppresses expression in the absence of tat (see. . .

DETDESC:

DETD(7)

The . . . folding enzymes, transport proteins, and the like), down-regulating host cell regulatory factors employed by the infectious agent (for example, the NF-.**kappa**.**B** **nuclear** **factor** found in activated lymphocytes which up-regulates HIV-1 transcription), up-regulating viral or host cell factors which suppress viral gene expression, by. . .

US PAT NO: 5,854,223 [IMAGE AVAILABLE] L15: 10 of 72
DATE ISSUED: Dec. 29, 1998
TITLE: S-DC28 as an antirestenosis agent after balloon injury
INVENTOR: Cy Stein, New City, NY
LeRoy Rabbani, New York, NY
ASSIGNEE: The Trustees of Columbia University in the City of New York, New York, NY (U.S. corp.)
APPL-NO: 08/678,234
DATE FILED: Jul. 11, 1996
ART-UNIT: 164
PRIM-EXMR: Scott W. Houtteman
LEGAL-REP: John P.Cooper & Dunham LLP White

US PAT NO: 5,854,223 [IMAGE AVAILABLE] L15: 10 of 72
US-CL-CURRENT: **514/44**; 536/24.5

DETDESC:

DETD(109)

In . . . non-sequence specifically inhibit fibronectin's binding to the .alpha.5.beta.1 integrin receptor present on phorbol-12, 13-myristat acetate Jurkat cells, which may induce **NF**-**KB** activity, thereby further reducing the ability of cells to adhere and spread [53]. Although the binding of PS oligos to. . .

US PAT NO: 5,849,286 [IMAGE AVAILABLE] L15: 11 of 72
DATE ISSUED: Dec. 15, 1998
TITLE: Ubiquitin conjugating enzymes 7,8 and 9
INVENTOR: Jian Ni, Gaithersburg, MD
Reiner Gentz, Silver Springs, MD
Mark D. Adams, North Potomac, MD
ASSIGNEE: Human Genome Sciences, Inc., Gaithersburg, MA (U.S. corp.)
APPL-NO: 08/464,604
DATE FILED: Jun. 5, 1995
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Lisa J. Hobbs
LEGAL-REP: Elliot M. Olstein, J. G. Mullins

US PAT NO: 5,849,286 [IMAGE AVAILABLE] L15: 11 of 72
US-CL-CURRENT: 424/94.5; 435/193; **514/12**

SUMMARY:

BSUM(10)

Maturation of the p105 **NF**-**KB** precursor into the active p50 subunit of the transcriptional activator also proceeds in a ubiquitin and proteasome-dependent manner. Furthermore, inhibitors to the proteasome block degradation of IkBa and thus prevent tumor necrosis factor alpha induced activation of **NF**-**KB** and its entry into the nucleus.

US PAT NO: 5,849,263 [IMAGE AVAILABLE] L15: 12 of 72
DATE ISSUED: Dec. 15, 1998
TITLE: Pharmaceutical compositions containing alkylaryl polyether alcohol polymer
INVENTOR: Thomas P. Kennedy, Richmond, VA
ASSIGNEE: Charlotte-Mecklenburg Hospital Authority, Charlotte, NC (U.S. corp.)
APPL-NO: 08/638,893
DATE FILED: Apr. 25, 1996
ART-UNIT: 166
PRIM-EXMR: Robert H. Harrison
LEGAL-REP: Bell Seltzer Intellectual Property Law Group of Alston & Bird LLP

US PAT NO: 5,849,263 [IMAGE AVAILABLE] L15: 12 of 72
US-CL-CURRENT: 424/45, 78.05, 78.06, 78.08, 78.37; **514/179**, **885**, **887**

SUMMARY:

BSUM(14)

These cytokines share regulation of their expression by the transcription factor **Nuclear** **Factor** **kappa**-**B** (NF-.**kappa**.B), a particularly important transcription factor mediating inflammatory events (U. Siebenlist, G. Granzuso and R. Brown. "Structure, regulation and function of. . . human peripheral blood mononuclear cells". International Journal of Immunology (1993) 6:409-422; R. Schreck, et al. "Dithiocarbamates as potent inhibitors of **nuclear** **factor** .**kappa**.**B** activation in intact cells". Journal of Experimental Medicine (1992) 175:1181-1194). However, the few antioxidants known to inhibit NF-.kappa.B activation share. . .

US PAT NO: 5,846,961 [IMAGE AVAILABLE] L15: 13 of 72
DATE ISSUED: Dec. 8, 1998
TITLE: Multi-faceted method to repress reproduction of latent viruses in humans and animals
INVENTOR: Knox Van Dyke, Morgantown, WV
ASSIGNEE: HIV Diagnostics, Inc., Lexington, KY (U.S. corp.)
APPL-NO: 08/479,010
DATE FILED: Jun. 7, 1995
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Price,Heneveld,Cooper,DeWitt & Litton

US PAT NO: 5,846,961 [IMAGE AVAILABLE] L15: 13 of 72
US-CL-CURRENT: **514/171**, **198**, **369**, **374**, **378**, **561**, **563**

ABSTRACT:
Disclosed . . . such as HIV, in animals by the generally concurrent administration of (1) antioxidants including a glutathione agent; and (2) an **NFKB** induction inhibitor. Also disclosed are pharmaceutical

compositions and kits for use in repressing reproduction of latent viruses such as HIV.

SUMMARY:

BSUM(8)

Schreck . . . The iKB factor is removed from the protein triad and the remaining p50, p65 complex becomes known as NF-kappa B (**NFKB**).

SUMMARY:

BSUM(9)

Schreck et al. have recognized that **NFKB** is a gene transcription factor that migrates into the nucleus of the HIV infected cell and switches on the production. . . expression of HIV-1 in a human T cell line. They further report that the expression of HIV is mediated by **NFKB** transcription factor which is potently and rapidly activated by a hydrogen peroxide treatment of cells from its inactive cytoplasmic form. They additionally report that N-acetyl cysteine and other thiol compounds block the activation of **NFKB**. They concluded that these diverse agents thought to activate **NFKB** by distinct intracellular pathways might act through a common mechanism involving the synthesis of reactive oxygen intermediates. They did not. . .

SUMMARY:

BSUM(10)

Sherman et al., Biochem. Biophys. Res. Comm., 191 (3):1301-1308, 1993, report that pyrrolidine dithiocarbamate (PDTC) is an inhibitor of **NFKB** activation. They further report that this compound is an inhibitor of nitric oxide synthase (NO synthase). They further report that. . . that PDTC may act as a scavenger of reactive oxygen species which prevents them from participation in the activation of **NFKB**.

SUMMARY:

BSUM(15)

The . . . the generally concurrent administration of 1) a glutathione agent; 2) at least one additional antioxidant; and 3) at least one **NFKB** induction inhibitor. Further aspects and advantages of the invention will be apparent to those skilled in the art upon review. . .

DETDESC:

DETD(3)

There . . . glutathione precursor, a glutathione production enhancer, or glutathione, (2) high doses of additional fat- and water-soluble antioxidants, and (3) an **NFKB** induction inhibitor, to an animal infected with a latent virus. The fat- and water-soluble antioxidants are administered to an animal. . .

DETDESC:

DETD(5)

The Role of **NFKB** and Peroxynitrite in the Activation of a Cell to Reproduce HIV **NFKB** is a gene transcription factor that switches on the production of the HIV virus of a virally infected cell. **NFKB** is known to activate a variety of genes, including the transcription of a variety of cytokines, viruses and NO Synthase.. . .

DETDESC:

DETD(9)

Peroxynitrite is significant in that it activates **NFKB**. **NFKB** is inactivated by I Kappa B (IKB) which acts on **NFKB** via the P65 subunit. As shown in FIG. 1, peroxynitrite cleaves IKB, thereby releasing the active **NFKB**.

DETDESC:

DETD(31)

NFKB Induction Inhibitors

DETDESC:

DETD(32)

NFKB induction inhibitors are agents that inhibit **NFKB** transcription factor from binding to DNA. This blocks the induction of HIV or other viral reproduction by directly suppressing the viral reproduction activating mechanism. **NFKB** inhibitors (item 7, FIG. 2) also suppress peroxynitrite synthesis, by preventing **NFKB** from activating cell genes to produce NO synthase.

DETDESC:

DETD(35)

The preferred type of **NFKB** induction inhibitor is an anti-inflammatory steroid. Examples of suitable anti-inflammatory steroids suitable as **NFKB** induction inhibitors include but are not limited to predonsone, prednisolone, methyl prednisolone, dexamethasone, beta metasone dehydroepiandrosterone, 9a-fluorocortisol, prednisone, aetiocholanolone, 2-methylcortisol, pregnanediol, deoxycorticosterone, cortisone, hydrocortisone (cortisol), 6a-methylprednisolone, triamcinolone, estrogen or derivatives thereof. Generally, any steroid with antiinflammatory action toward **NFKB** may be used. In addition, one or more suitable nonglucocorticoid lazaroids may be utilized as **NFKB** induction inhibitors. Preferred lazaroids include, but are not limited to, U-74006F, which is 21-[4-(2,6-di-1-pyrrolidinyl-4-pyrimidinyl)---piperazinyl] -16-methyl-(16alpha.)-pregna-1,4,9(11)triene-3,20-dione monomethanesulfonate or TIRILAZAD mesylate or. . .

DETDESC:

DETD(39)

In . . . weight. Other antiinflammatory steroids can be substituted at appropriate doses, as set forth in the Physicians'Desk Reference. Adminstration of an **NFKB** induction inhibitor such as an anti-inflammatory steroid, is one of the most important steps in the treatment of HIV, AIDS. . .

DETDESC:

DETD(43)

In addition, to the previously noted anti-inflammatory steroids and lazaroids, a variety of other compounds may be utilized as **NFKB** induction inhibitors such as pyrrolidine dithiocarbamate and other dithiocarbamates, and glycyrrhizic acid (from licorice root). A preferred dosage level when. . . is about 100 mg/day per person for each day of therapy. In addition, other compounds are suitable for use as **NFKB** induction inhibitors. These inhibitors include, but are not limited to, immunosuppressants such as cyclosporin A, rapamycin, interleukin 10, and FK. . . Clearly, a wide array of plant steroids, male steroids, female steroids, glucocorticoids, lazaroids, and 21-aminosteroids are eligible for use as **NFKB** induction inhibitors.

DETDESC:

DETD(44)

An inhibitor known to be effective against **NFKB** binding or expressing is mevinolin, a drug which prevents isoprenylation and methylthioadenosine (MTA) and inhibitor of several S adenosylmethionine dependent. . .

DETDESC:

DETD(51)

Although . . . antioxidants, glutathione agents, and steroids with regard to HIV production. HIV replication is blocked by a combination of antioxidants and **NFKB** induction inhibitor. About 7% of the blocking action of HIV replication is believed to stem from the **NFKB** induction inhibitor, which preferably is one or more anti-inflammatory steroids. Although such steroids do not have direct inhibitory activity, they control viral synthesis by blocking **NFKB** induction. As will be recalled, **NFKB** is a DNA transcription factor made of protein. **NFKB** controls a whole series of inflammatory cytokines and NO synthase as well as HIV and FIV replication. Upon introduction of. . .

DETDESC:

DETD(52)

However, for **NFKB** to be active it must shed its inhibitory factor I kappa B. Such shedding requires oxidation because the bonds holding. . . to proteins P50 and P65 are sensitive to oxidation. Thus, antioxidants keep the I kappa B inhibitory factor bound to **NFKB** and therefore inactive. The role of antioxidants in the mechanism depicted in FIG. 3 is believed to be responsible for about 30% of the activity of producing **NFKB**, and preventing HIV replication.

DETDESC:

DETD(53)

All . . . known to those skilled in the art. Although it is most preferred to administer the anitoxidants including glutathione agent and **NFKB** induction inhibitor concurrently, or simultaneously, it is not a

requirement. Thus, the preferred embodiments of the present invention also encompass. . .

DETDESC:

DETD(55)

The . . . a glutathione agent; (2) an effective amount of one or more additional antioxidants; and (3) an effective amount of an **NFKB** induction inhibitor. In a most preferred embodiment, the pharmaceutical compositions comprise: (1) an effective amount of a glutathione agent, e.g.. . . antioxidant, (2b) an effective amount of a fat-soluble antioxidant, and (3) an effective amount of an anti-inflammatory steroid as the **NFKB** induction inhibitor. The other ingredients described above may also be included.

DETDESC:

DETD(62)

In . . . C, A and E; an effective amount of at least one glutathione precursor such as N-acetyl cysteine; followed by an **NFKB** induction inhibitor such as one or more anti-inflammatory steroids or lazaroids. As summarized in Table 4 below, seven cats heavily. . . 10 to about 18 pounds. The cats were initially treated with a single dosage of an effective amount of an **NFKB** induction inhibitor, that is an antiinflammatory steroid dose of DEPO-MEDROL (20-25 mg) and a series of oral dosages of a. . .

DETDESC:

DETD(66)

In . . . fat-soluble antioxidants and an effective amount of at least one glutathione precursor such as N-acetyl cysteine are administered. Before an **NFKB** induction inhibitor is administered, the CD.sub.4 (T-lymphocyte) count is increased to about 100 cells/mm.sup.3 or more. The CD.sub.4 count may. . . concentrates containing monocytes may be given, such as via transfusions. Once CD.sub.4 counts are about 100 cells/mm.sup.3 or more, an **NFKB** induction inhibitor is administered.

DETDESC:

DETD(67)

In both the preferred and optional treatment regimens, the **NFKB** induction inhibitor is administered until AIDS(-) is indicated from AIDS(+) blood assay, via ELISA, Western blot, and PCR (polymerase chain. . .

DETDESC:

DETD(78)

Preferably, . . . suitable glutathione precursors could be utilized in place of, or instead of the N-acetyl cysteine. Similarly, one or more other **NFKB** induction inhibitors could be utilized in place of or instead of the methyl prednisolone.

DETDESC:

DETD(81)

The . . . one fat soluble antioxidant at doses higher than the recommended daily minimum requirements, and preferably, only slight amounts or no **NFKB** induction inhibitor. In a most preferred treatment regimen, the subject suffering from symptoms of the Herpes virus is administered generally. . .

CLAIMS:

CLMS(1)

The . . .
combinations thereof,
ii) at least one additional antioxidant at doses higher than the recommended daily minimum requirements; and
iii) at least one **NFKB** induction inhibitor in an amount effective to inhibit **nuclear** **factor** **kappa** **B**; said at least one **NFKB** induction inhibitor being selected from the group consisting of anti-inflammatory steroids and nonglucocorticoid lazaroids.

CLAIMS:

CLMS(11)

11. The method of claim 1 wherein said **NFKB** induction inhibitor comprises at least one anti-inflammatory steroid.

CLAIMS:

CLMS(13)

13. The method of claim 1 wherein said **NFKB** induction inhibitor comprises a nonglucocorticoid lazaroid.

CLAIMS:

CLMS(15)

15. The method of claim 1 further comprising administering:
iv) a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

CLAIMS:

CLMS(17)

17. . . .
combinations thereof;
ii) at least one additional antioxidant at doses higher than the recommended daily minimum requirements; and
iii) at least one **NFKB** induction inhibitor in an amount effective to inhibit **nuclear** **factor** **kappa** **B**; said at least one **NFKB** induction inhibitor being selected from the group consisting of anti-inflammatory steroids and nonglucocorticoid lazaroids.

CLAIMS:

CLMS(27)

27. The method of claim 17 wherein said **NFKB** induction inhibitor comprises at least one anti-inflammatory steroid.

CLAIMS:

CLMS(29)

29. The method of claim 17 wherein said **NFKB** induction inhibitor comprises a nonglucocorticoid lazaroid.

CLAIMS:

CLMS(31)

31. The method of claim 17 further comprising administering:
iv) a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

US PAT NO: 5,846,959 [IMAGE AVAILABLE] L15: 14 of 72
DATE ISSUED: Dec. 8, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/471,537
DATE FILED: Jun. 6, 1995
ART-UNIT: 161
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,846,959 [IMAGE AVAILABLE] L15: 14 of 72
US-CL-CURRENT: **514/165**; 424/9.1, 9.2; 435/6, 7.2, 7.21, 7.24, 7.94, 7.95; 436/71, 86, 129, 172, 503, 504, 548; **514/18**, **171**, **211**, **423**, **457**, **478**, **479**

SUMMARY:

BSUM(5)

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(6)

Importantly, the activation of **NF**-**kB** in vascular endothelial

cells by diverse signals can be specifically inhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. RAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEc by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(55)

Linoleic Acid Induces Transcriptional Activation of the VCAM-1 Promoter by a Redox-Sensitive **NF**-**kB** Like Factor

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha... .

DETDESC:

DETD(59)

Polyunsaturated Fatty Acids Activate **NF**-**kB**-like DNA Binding Activities that are Blocked by the Antioxidant PDTC

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

US PAT NO: 5,843,643 [IMAGE AVAILABLE] L15: 15 of 72
DATE ISSUED: Dec. 1, 1998
TITLE: Site-specific transfection of eukaryotic cells using polypeptide-linked recombinant nucleic acid
INVENTOR: Paul L. Ratner, 11 Ash St., Bar Harbor, ME 04609
APPL-NO: 08/199,608
DATE FILED: Feb. 22, 1994
ART-UNIT: 187
PRIM-EXMR: W. Gary Jones
ASST-EXMR: Dianne Rees
LEGAL-REP: Patrick D. Kelly

US PAT NO: 5,843,643 [IMAGE AVAILABLE] L15: 15 of 72
US-CL-CURRENT: 435/6, 5, 91.1; **514/2**, **44**; 530/300, 350; 536/23.1, 24.3, 24.5

DETDESC:

DETD(12)

. . .

SRF c-fos oncogene

Thyroid hormone
Growth hormone

receptor
CREB Somatostatin Singh et al 1989
NF-**kB** Human immunodeficiency virus

YB-1 Major histocompatibility II

GATA-1 Beta globin Trainor et al 1990
GCF Epidermal. . .

DETDESC:

DETD(246)

. . .

linear
(ii) MOLECULE TYPE: DNA (genomic)
(iii) HYPOTHETICAL: NO
(iv) ANTI-SENSE: NO
(vi) ORIGINAL SOURCE:
(A) ORGANISM: binding site for **NF**-**KB** chromosome binding protein
(B) STRAIN: human
(F) TISSUE TYPE: human
(G) CELL TYPE: human
(x) PUBLICATION INFORMATION:
(A) AUTHORS: Singh,. . .

US PAT NO: 5,840,710 [IMAGE AVAILABLE] L15: 16 of 72
DATE ISSUED: Nov. 24, 1998
TITLE: Cationic amphiphiles containing ester or ether-linked lipophilic groups for intracellular delivery of therapeutic molecules
INVENTOR: Edward R. Lee, Quincy, MA
David J. Harris, Lexington, MA
Craig S. Siegel, Woburn, MA
Mathieu B. Lane, Cambridge, MA
Shirley C. Hubbard, Belmont, MA
Seng H. Cheng, Wellesley, MA
Simon J. Eastman, Marlboro, MA
John Marshall, Milford, MA
Ronald K. Scheule, Hopkinton, MA
ASSIGNEE: Genzyme Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/546,087
DATE FILED: Oct. 20, 1995
ART-UNIT: 189
PRIM-EXMR: Bruce R. Campbell
LEGAL-REP: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

US PAT NO: 5,840,710 [IMAGE AVAILABLE] L15: 16 of 72

US-CL-CURRENT: **514/44**; 424/450; **514/2**; 554/1, 227; 560/1, 224

DETDESC:

DETD(285)

It . . . increase with the severity of an inflammatory condition (for example, tumor necrosis factor "TNF" and potentially transcription factors such as **NF**-**kB**, AP-1, NF-IL6 and octamer binding protein). It has also been determined that interleukin 8, a polypeptide of 8,500 MW, is. . .

US PAT NO: 5,840,277 [IMAGE AVAILABLE] L15: 17 of 72
DATE ISSUED: Nov. 24, 1998
TITLE: Treatment of chronic pulmonary inflammation
INVENTOR: Andrew J. Ghio, Durham, NC
Thomas P. Kennedy, Richmond, VA
ASSIGNEE: Charlotte Hospital Authority, Charlotte, NC (U.S. corp.)
APPL-NO: 08/632,275
DATE FILED: Apr. 15, 1996
ART-UNIT: 185
PRIM-EXMR: David Guzo
LEGAL-REP: The Bell Seltzer Intellectual Law Firm of Alston & Bird, LLP

US PAT NO: 5,840,277 [IMAGE AVAILABLE] L15: 17 of 72
US-CL-CURRENT: 424/45, 78.05, 78.37; **514/828**, **851**

SUMMARY:

BSUM(3)

The . . . inflammation. More particularly, the present invention relates to the use of alkylaryl polyether alcohol polymers to reduce the activation of **nuclear** **factor** **kappa** **B** (NF-.**kappa**.B) and inhibit the secretion of pro-inflammatory cytokines TNF-alpha (TNF-.alpha.), interleukin-1 beta (IL-1.beta.), interleukin-6 (IL-6), interleukin-8 (IL-8) and the growth factor. . .

SUMMARY:

BSUM(15)

These cytokines share regulation of their expression by the transcription factor **Nuclear** **Factor** **kappa**-**B** (NF-.**kappa**.B), a particularly important transcription factor mediating inflammatory events (U. Siebenlist, G. Granzuso and R. Brown. "Structure, regulation and function of. . . human peripheral blood mononuclear cells". International Journal of Immunology (1993) 6:409-422; R. Schreck, et al. "Dithiocarbamates as potent inhibitors of **nuclear** **factor** .**kappa**.**B** activation in intact cells". Journal of Experimental Medicine (1992) 175:1181-1194). However, the few antioxidants known to inhibit NF-.kappa.B activation share. . .

US PAT NO: 5,837,510 [IMAGE AVAILABLE] L15: 18 of 72
DATE ISSUED: Nov. 17, 1998
TITLE: Methods and polynucleotide constructs for treating host cells for infection or hyperproliferative disorders
INVENTOR: Mark A. Goldsmith, 263 Chenery St., San Francisco, CA 94131
Robert O. Ralston, 2863 Judah, San Francisco, CA 94122
APPL-NO: 08/472,056
DATE FILED: Jun. 6, 1995
ART-UNIT: 185
PRIM-EXMR: Johnny Railey
LEGAL-REP: Norman J. Kruse, Donald J. Pochopien, Robert P. Blackburn

US PAT NO: 5,837,510 [IMAGE AVAILABLE] L15: 18 of 72
US-CL-CURRENT: 435/455; 424/93.2; 435/320.1, 456; **514/44**; 536/23.1, 23.2, 23.5, 23.53, 23.6, 23.7, 23.72, 24.1, 24.5

DETDESC:

DETD(6)

The . . . contains both the tar region, which is highly selective for HIV tat, and also a region activated by the endogenous **nuclear** **factor** NF-.sub..**kappa**. **B** (the LTR has tandem NF-.sub..kappa. B binding regions). Although the tar sequence strongly suppresses expression in the absence of tat. . .

DETDESC:

DETD(7)

The . . . folding enzymes, transport proteins, and the like), down-regulating host cell regulatory factors employed by the infectious agent (for example, -the NF-.sub..**kappa**. **B** **nuclear** **factor** found in activated lymphocytes which up-regulates HIV-1 transcription), up-regulating viral or host cell factors which suppress viral gene expression, by. . .

US PAT NO: 5,830,848 [IMAGE AVAILABLE] L15: 19 of 72
DATE ISSUED: Nov. 3, 1998
TITLE: Method and agents for inducement of endogenous nitric oxide synthase for control and management of labor during pregnancy
INVENTOR: Michael R. Harrison, San Francisco, CA
Michael A. Heymann, San Francisco, CA
Robert Kirk Riemer, Half Moon Bay, CA
Eileen Stack Natuzzi, San Francisco, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/450,126
DATE FILED: May 25, 1995
ART-UNIT: 182
PRIM-EXMR: Stephen Walsh
ASST-EXMR: Daryl A. Basham
LEGAL-REP: Hana Verny

US PAT NO: 5,830,848 [IMAGE AVAILABLE] L15: 19 of 72
US-CL-CURRENT: **514/2**; 424/85.1, 85.2, 85.5; 530/399

DETDESC:

DETD(25)

Additionally, . . . on NO production augmentation. These agents are putative control elements which modify the expression of transcriptional regulatory proteins such as **nuclear** **factor** NF **Kappa** **B** Jun/fos, tumor necrosis factor (TNT-.alpha.), NF-116, activator protein (AP-1), octamer binding protein, (OCT-1), (OCT-2), PU-1, and gamma activation factor (GAF),. . .

CLAIMS:

CLMS(19)

19. The method of claim 1 wherein the transcriptional regulating protein is **nuclear** **factor** **kappa** **B** Jun/fos.

US PAT NO: 5,824,664 [IMAGE AVAILABLE] L15: 20 of 72
DATE ISSUED: Oct. 20, 1998
TITLE: Suppression of HIV expression by organic thiophosphate
INVENTOR: Philip S. Schein, Bryn Mawr, PA
Thea Kalebic, Bethesda, MD
ASSIGNEE: U.S. Bioscience, Inc., West Conshohocken, PA (U.S. corp.)
National Institutes of Health, The National Cancer Institute, Rockville, MD (U.S. corp.)
APPL-NO: 08/037,633
DATE FILED: Mar. 26, 1993
ART-UNIT: 188
PRIM-EXMR: Leon B. Lankford, Jr.
ASST-EXMR: Francisco C. Prats
LEGAL-REP: Pennie & Edmonds LLP

US PAT NO: 5,824,664 [IMAGE AVAILABLE] L15: 20 of 72
US-CL-CURRENT: **514/143**, **75**, **114**, **665**

DETDESC:

DETD(73)

Similar to N-acetyl cysteine, which suppressed PMA- and TNF.alpha.-mediated induction of HIV-LTR transcription by inhibiting **NFKB** activity (Staal, F. J. et al., 1990, supra), WR 151327 suppressed transcriptional activity of HIV-LTR in transiently transfected RD cells.. . .

US PAT NO: 5,821,260 [IMAGE AVAILABLE] L15: 21 of 72
DATE ISSUED: Oct. 13, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/485,307
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,821,260 [IMAGE AVAILABLE] L15: 21 of 72

US-CL-CURRENT: **514/423**; 424/9.1, 9.2; 435/6, 7.2, 7.21, 7.24, 7.94, 7.95; 436/71, 86, 129, 172, 503, 504, 548; **514/18**, **226.2**, **477**, **478**, **479**, **484**, **485**, **487**

DETDESC:

DETD(63)

At the molecular level, PDTC has been shown to inhibit the activation of the transcriptional regulatory factor **Nf**-**kB** in response to certain cytokine and non-cytokine stimuli (Schreck, Rieber et al. 1991; Schreck, Meier et al. 1992). However, by. . . has been discovered that endothelial cells activate VCAM-1 gene expression through an apparently novel transcriptional regulatory factor that is not **Nf**-**kB**. This suggests that PDTC may regulate endothelial cell gene expression through its effect on a new transcriptional regulatory protein. It. . .

US PAT NO: 5,814,612 [IMAGE AVAILABLE] L15: 22 of 72
DATE ISSUED: Sep. 29, 1998
TITLE: Retinol derivatives and uses thereof
INVENTOR: Jochen Buck, New York, NY
Ulrich Hammerling, New York, NY
Fadila Derguini, New York, NY
Koji Nakanishi, New York, NY
ASSIGNEE: Sloan-Kettering Institute for Cancer Research, New York, NY (U.S. corp.)
The Trustees of Columbia in the City of New York, New York, NY (U.S. corp.)
APPL-NO: 07/880,041
DATE FILED: May 6, 1992
ART-UNIT: 126
PRIM-EXMR: Johann Richter
ASST-EXMR: John Peabody
LEGAL-REP: John P. White

US PAT NO: 5,814,612 [IMAGE AVAILABLE] L15: 22 of 72
US-CL-CURRENT: **514/21**, **725**; 549/453, 512, 551, 554, 561, 563; 552/10, 11, 12; 558/430; 562/867; **564/123**, **152**, **153**; 568/823, 824, 825

DETDESC:

DETD(81)

The . . . molecules, that shuttle to the nucleus to regulate transcription. For example, the protein products of the rel gene family (e.g., **NF**-**kB**) translocate upon activation from the cytoplasm to the nucleus and regulate transcription (24). Small lipophilic molecules including the steroids, vitamin. . .

US PAT NO: 5,811,449 [IMAGE AVAILABLE] L15: 23 of 72
DATE ISSUED: Sep. 22, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Altanta, GA (U.S. corp.)
APPL-NO: 08/483,335
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,811,449 [IMAGE AVAILABLE] L15: 23 of 72
US-CL-CURRENT: **514/423**; 424/9.1, 9.2; 436/71, 86, 129; **514/18**, **226.2**, **477**, **478**, **479**, **484**, **485**, **487**, **488**, **489**, **506**, **513**, **517**, **518**, **553**, **561**, **824**, **825**, **826**, **861**, **863**; 530/331; 548/431, 531; 549/10; 558/230, 234, 235, 250; 562/26, 27; **564/76**; 568/21, 25

SUMMARY:

BSUM(5)

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(6)

Importantly, the activation of **NF**-**kB** in vascular endothelial cells by diverse signals can be specifically hinhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. HAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEC by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(55)

Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces

transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha... .

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

US PAT NO: 5,807,884 [IMAGE AVAILABLE] L15: 24 of 72
DATE ISSUED: Sep. 15, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/317,399
DATE FILED: Oct. 4, 1994
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,807,884 [IMAGE AVAILABLE] L15: 24 of 72
US-CL-CURRENT: **514/423**, **488**, **489**, **506**, **513**, **517**, **518**, **553**, **561**, **824**, **825**, **826**, **861**, **863**; 530/331; 548/431; 549/16

SUMMARY:

BSUM(3)

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(4)

Importantly, the activation of **NF**-**kB** in vascular endothelial cells by diverse signals can be specifically inhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. HAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEC by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(55)

Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor.

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha... .

DETDESC:

DETD(59)

Polyunsaturated Fatty Acids Activate **NF**-**kB**-like DNA Binding Activities that are Blocked by the Antioxidant PDTC.

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(61)

FIG. 8 illustrates that linoleic acid induces **NF**-**kB** binding activity to VCAM-1 promotor in a redox-sensitive manner. This is analogous to cytokine TNF-.alpha. and suggests a similar mechanism. . .

US PAT NO: 5,807,746 [IMAGE AVAILABLE] L15: 25 of 72
DATE ISSUED: Sep. 15, 1998
TITLE: Method for importing biologically active molecules into cells
INVENTOR: Yao-Zhong Lin, Nashville, TN
Jack J. Hawiger, Nashville, TN
ASSIGNEE: Vanderbilt University, Nashville, TN (U.S. corp.)
APPL-NO: 08/258,852
DATE FILED: Jun. 13, 1994
ART-UNIT: 185
PRIM-EXMR: Nancy Degen
LEGAL-REP: Needle & Rosenberg

US PAT NO: 5,807,746 [IMAGE AVAILABLE] L15: 25 of 72
US-CL-CURRENT: 435/375; **514/1**, **2**, **21**; 530/300, 350

DETDESC:

DETD(70)

Having . . . attached to the amino-terminal hydrophobic sequence conferring membrane-permeable capacity. For this purpose a sequence representing a functional domain of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B) responsible for a nuclear localization signal was selected. Import of such a peptide into the cell would be measured by. . .

US PAT NO: 5,801,195 [IMAGE AVAILABLE] L15: 26 of 72
DATE ISSUED: Sep. 1, 1998
TITLE: Immunotherapeutic aryl amides
INVENTOR: George W. Muller, Bridgewater, NJ
Mary Shire, North Plainfield, NJ
David I. Stirling, Branchburg, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/366,618
DATE FILED: Dec. 30, 1994
ART-UNIT: 123
PRIM-EXMR: Jane Fan
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,801,195 [IMAGE AVAILABLE] L15: 26 of 72
US-CL-CURRENT: **514/539**, **532**, **534**, **616**, **617**, **618**, **619**, **622**; 560/39, 41, 42; **564/155**, **158**, **169**, **170**, **176**, **180**, **182**, **183**, **219**, **220**

SUMMARY:

BSUM(14)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,798,368 [IMAGE AVAILABLE] L15: 27 of 72
DATE ISSUED: Aug. 25, 1998
TITLE: Tetrasubstituted 2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolines and method of reducing TNF.alpha. levels
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger Shen-Chu Chen, Edison, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/701,494
DATE FILED: Aug. 22, 1996
ART-UNIT: 164
PRIM-EXMR: James H. Reamer
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,798,368 [IMAGE AVAILABLE] L15: 27 of 72
US-CL-CURRENT: **514/323**; 546/201

SUMMARY:

BSUM(11)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,795,876 [IMAGE AVAILABLE] L15: 28 of 72
DATE ISSUED: Aug. 18, 1998
TITLE: Method of inhibiting vascular cell adhesion molecule-1 and treating chronic inflammatory diseases with 2, 6-di-alkyl-4-silyl-phenols
INVENTOR: Paul S. Wright, Cincinnati, OH
Steven J. Busch, West Chester, OH
ASSIGNEE: Hoechst Marion Rousssel, Inc., Cincinnati, OH (U.S. corp.)
APPL-NO: 08/824,221
DATE FILED: Mar. 25, 1997
ART-UNIT: 164
PRIM-EXMR: Phyllis G. Spivack
LEGAL-REP: William R. Boudreaux, David M. Stemerick

US PAT NO: 5,795,876 [IMAGE AVAILABLE] L15: 28 of 72
US-CL-CURRENT: **514/63**

SUMMARY:

BSUM(6)

The . . . have been cloned and characterized. For example, both promoters contain multiple DNA sequence elements which can bind the transcription factor, **NF**-**kB**. Iademarco, M. F. et al., J. Biol. Chem. 267, 16323-16329 (1992); Voraberger, G. et al., J. Immunol. 147, 2777-2786 (1991). The **NF**-**kB** family of transcription factors is central in the regulation of several genes upregulated within sites of inflammation. The activation of **NF**-**kB** as a transcription factor involves dissociation from an inhibitory subunit, IkB, in the cytoplasm. **NF**-**kB** subunits translocate to the nucleus, bind to specific DNA sequence elements, and activate transcription of several genes, including VCAM-1 and. . .

US PAT NO: 5,792,787 [IMAGE AVAILABLE] L15: 29 of 72
DATE ISSUED: Aug. 11, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/486,239
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,792,787 [IMAGE AVAILABLE] L15: 29 of 72
US-CL-CURRENT: **514/423**, **210**, **315**, **478**, **479**, **484**, **485**, **487**, **488**, **489**, **506**, **513**, **824**, **825**, **826**, **861**, **863**; 546/245; 548/531, 953; 558/230, 235

DETDESC:

DETD(28)

At the molecular level, PDTC has been shown to inhibit the activation of the transcriptional regulatory factor **Nf**-**kB** in response to certain cytokine and non-cytokine stimuli (Schreck, Rieber et al..1991; Schreck, Meier et al. 1992). However, by. . . has been discovered that endothelial cells activate VCAM-1 gene expression through an apparently novel transcriptional regulatory factor that is not **Nf**-**kB**. This suggests that PDTC may regulate endothelial cell gene expression through its effect on a new transcriptional regulatory protein. It. . .

US PAT NO: 5,783,596 [IMAGE AVAILABLE] L15: 30 of 72
DATE ISSUED: Jul. 21, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/477,881
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,783,596 [IMAGE AVAILABLE] L15: 30 of 72
US-CL-CURRENT: **514/423**; 424/9.1, 9.2; 436/71, 86, 129; **514/18**, **226.2**, **477**, **478**, **479**, **484**, **485**, **487**, **488**, **489**, **506**, **513**, **517**, **518**, **553**, **561**, **824**, **825**, **826**, **861**, **863**; 530/331; 548/431, 531; 549/10; 558/230, 234, 235, 250; 562/26, 27; **564/76**; 568/21, 25

DETDESC:

DETD(56)

At the molecular level, PDTC has been shown to inhibit the activation of the transcriptional regulatory factor **Nf**-**kB** in response to certain cytokine and non-cytokine stimuli (Schreck, Rieber et al. 1991; Schreck, Meier et al. 1992). However, by. . . has been discovered that endothelial cells activate VCAM-1 gene expression through an apparently novel transcriptional regulatory factor that is not **Nf**-**kB**. This suggests that PDTC may regulate endothelial cell gene expression through its effect on a new transcriptional regulatory protein. It. . .

US PAT NO: 5,783,565 [IMAGE AVAILABLE] L15: 31 of 72
DATE ISSUED: Jul. 21, 1998

TITLE: Cationic amphiphiles containing spermine or spermidine cationic group for intracellular delivery of therapeutic molecules
INVENTOR: Edward R. Lee, Quincy, MA
David J. Harris, Lexington, MA
Craig S. Siegel, Woburn, MA
Seng H. Cheng, Wellesley, MA
Simon J. Eastman, Marlboro, MA
John Marshall, Milford, MA
Ronald K. Scheule, Hopkinton, MA
ASSIGNEE: Genzyme Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/595,375
DATE FILED: Feb. 1, 1996
ART-UNIT: 189
PRIM-EXMR: Jasemine C. Chambers
ASST-EXMR: Abdur Razzaque
LEGAL-REP: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

US PAT NO: 5,783,565 [IMAGE AVAILABLE] L15: 31 of 72
US-CL-CURRENT: **514/44**; 424/450; 536/23.1; 552/544

DETDESC:

DETD(297)

It . . . increase with the severity of an inflammatory condition (for example, tumor necrosis factor "TNF" and potentially transcription factors such as **NF**-**kB**, AP-1, NF-IL6 and octamer binding protein). It has also been determined that interleukin 8, a polypeptide of 8,500 MW, is. . .

US PAT NO: 5,780,220 [IMAGE AVAILABLE] L15: 32 of 72
DATE ISSUED: Jul. 14, 1998
TITLE: Methods and compositions for inhibiting HIV replication
INVENTOR: David B. Weiner, Merion, PA
Yosef Refaeli, Boston, MA
David N. Levy, Birmingham, AL
ASSIGNEE: Trustees of the University of Pennsylvania, Philadelphia, PA (U.S. corp.)
APPL-NO: 08/382,873
DATE FILED: Feb. 3, 1995
ART-UNIT: 188
PRIM-EXMR: Laurie Scheiner
ASST-EXMR: Jeffrey S. Parkin
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris, LLP

US PAT NO: 5,780,220 [IMAGE AVAILABLE] L15: 32 of 72
US-CL-CURRENT: 435/5; 424/188.1; 435/7.1; **514/49**, **51**, **179**; 530/350

SUMMARY:

BSUM(10)

The . . . infection of myeloid cell lines can result in a more differentiated phenotype and increase the expression of factors such as **NF**-**KB** which are necessary for HIV replication. Roulston, A. et al. (1992) J. Exp. Med. 175:751; and Chantal Petit, A. J.. . .

US PAT NO: 5,773,231 [IMAGE AVAILABLE] L15: 33 of 72
DATE ISSUED: Jun. 30, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/473,272
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M.King & Spalding Knowles

US PAT NO: 5,773,231 [IMAGE AVAILABLE] L15: 33 of 72
US-CL-CURRENT: 435/7.24; **514/489**, **506**, **513**, **824**, **825**, **826**, **861**, **863**; 530/331; 548/431; 558/230, 235; **564/76**; 568/21, 25

SUMMARY:

BSUM(4)

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(5)

Importantly, the activation of **NF**-**kB** in vascular endothelial cells by diverse signals can be specifically inhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. HAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEC by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(55)

Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor.

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha... .

DETDESC:

DETD(59)

Polyunsaturated Fatty Acids Activate **NF**-**kB**-like DNA Binding Activities that are Blocked by the Antioxidant PDTC.

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(61)

FIG. 8 illustrates that linoleic acid induces **NF**-**kB** binding activity to VCAM-1 promotor in a redox-sensitive manner. This is analogous to cytokine TNF-.alpha. and suggests a similar mechanism. . .

US PAT NO: 5,773,209 [IMAGE AVAILABLE] L15: 34 of 72
DATE ISSUED: Jun. 30, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/484,059
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M.King & Spalding Knowles

US PAT NO: 5,773,209 [IMAGE AVAILABLE] L15: 34 of 72
US-CL-CURRENT: 435/7.24; 424/9.1, 9.2; 435/6, 7.2, 7.21, 7.94, 7.95; 436/71, 86, 129, 172, 503, 504, 548; **514/18**, **423**, **478**, **479**, **484**, **485**, **487**, **488**

SUMMARY:

BSUM(5),

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(6)

Importantly, the activation of **NF**-**kB** in vascular endothelial cells by diverse signals can be specifically inhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. HAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEC by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(55)
Linoleic Acid Induces Transcriptional Activation of the VCAM-1 Promoter by a Redox-sensitive **NF**-**kB** Like Factor

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha... .

DETDESC:

DETD(59)
Polyunsaturated Fatty Acids Activate **NF**-**kB**-like DNA Binding Activities that are Blocked by the Antioxidant PDTC

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

US PAT NO: 5,770,581 [IMAGE AVAILABLE] L15: 35 of 72
DATE ISSUED: Jun. 23, 1998

TITLE: Gene transcription and ionizing radiation: methods and compositions
INVENTOR: Ralph R. Weichselbaum, Chicago, IL
Dennis E. Hallahan, Park Ridge, IL
Vikas P. Sukhatme, Chicago, IL
Donald W. Kufe, Wellesley, MA
ASSIGNEE: Arch Development Corp., Chicago, IL (U.S. corp.)
Dana-Farber Cancer Institute, Boston, MA (U.S. corp.)
APPL-NO: 08/474,445
DATE FILED: Jun. 7, 1995
ART-UNIT: 189
PRIM-EXMR: Bruce R. Campbell
LEGAL-REP: Arnold, White & Durkee

US PAT NO: 5,770,581 [IMAGE AVAILABLE] L15: 35 of 72
US-CL-CURRENT: **514/44**; 435/447, 455; 536/24.1

DETDESC:

DETD(85)

Transcription . . . domains are well known in the art. Exemplary transcription factors having activation domains are GAL4, c-Jun, viral protein VP-16, and **nuclear** **factor** NF-.**kappa**.**B**.

DETDESC:

DETD(100)

Nuclear **factor** NF-.**kappa**.**B** is a transcription factor. The activation domain of NF-.kappa.B comprises amino acid residue sequences from about residue position 414 to. . .

DETDESC:

DETD(272)

The . . . al., 1990; Hallahan, et al, 1991). Other studies have demonstrated that x-rays induce expression and DNA binding activity of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B; Brach, et al., 1991).

DETDESC:

DETD(315)

Ionizing . . . which code for transcription factors. Other studies have demonstrated that ionizing radiation induces expression and DNA binding activity of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B). The activation of transcription factors likely represents a critical control point in transducing early nuclear signals to longer term changes. . .

DETDESC:

DETD(330)

NAC . . . phorbol ester-induced activation of the HIV-1 long terminal repeat. This antioxidant has also been found to inhibit activation of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B) by phorbol esters and other agents such as H.sub.2 O.sub.2. The available findings suggest the release activate NF-.kappa.B by induced. . .

US PAT NO: 5,767,099 [IMAGE AVAILABLE] L15: 36 of 72
DATE ISSUED: Jun. 16, 1998
TITLE: Cationic amphiphiles containing amino acid or dervatized amino acid groups for intracellular delivery of therapeutic molecules
INVENTOR: David J. Harris, Lexington, MA
Edward R. Lee, Quincy, MA
Craig S. Siegel, Woburn, MA
Eric A. Rowe, Malden, MA
Shirley C. Hubbard, Belmont, MA
ASSIGNEE: Genzyme Corporation, Cambridge, MA (U.S. corp.)
APPL-NO: 08/546,086
DATE FILED: Oct. 20, 1995
ART-UNIT: 184
PRIM-EXMR: Jacqueline M. Stone
ASST-EXMR: Patrick Twomey
LEGAL-REP: E. Victor Donahue

US PAT NO: 5,767,099 [IMAGE AVAILABLE] L15: 36 of 72
US-CL-CURRENT: **514/44**, **182**, **777**; 516/915; 552/544; 560/6

DETDESC:

DETD(297)

It . . . increase with the severity of an inflammatory condition (for example, tumor necrosis factor "TNF" and potentially transcription factors such as **NF**-**kB**, AP-1, NF-IL6 and octamer binding protein). It has also been determined that interleukin 8, a polypeptide of 8,500 MW, is. . .

US PAT NO: 5,750,351 [IMAGE AVAILABLE] L15: 37 of 72
DATE ISSUED: May 12, 1998
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
Sampath Parthasarathy, Atlanta, GA
Bobby V. Khan, Dunwoody, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 08/474,530
DATE FILED: Jun. 7, 1995
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan
LEGAL-REP: Sherry M. Knowles, JacquelineKing & Spalding Haley

US PAT NO: 5,750,351 [IMAGE AVAILABLE] L15: 37 of 72
US-CL-CURRENT: 435/7.21; 424/9.1, 9.2; 435/6, 7.2, 7.24, 7.94, 7.95; 436/71, 86, 129, 172, 503, 504, 548; **514/18**, **226.2**, **423**, **477**, **478**, **479**, **484**, **485**, **487**, **488**, **489**, **506**, **513**, **517**, **518**, **553**, **561**, **824**, **825**, **826**, **861**, **863**; 530/331; 548/431; 549/16; 558/230, 234, 235, 250; 562/26, 27; **564/76**

SUMMARY:

BSUM(4)

Molecular . . . of the regulatory elements on the human VCAM-1 gene that control its expression suggests an important role for nuclear factor-kB (**NF**-**kB**), a transcriptional regulatory factor, or an NF-k.beta. like binding protein in oxidation-reduction-sensitive regulation of VCAM-1 gene expression. Transcriptional factors are. . . role in mediating inflammatory and other stress signals to the nuclear regulatory apparatus. Although the precise biochemical signals that activate **NF**-**kB** are unknown, this transcriptional factor may integrate into a common molecular pathway many of the risk factors and "causative" signals. . .

SUMMARY:

BSUM(5)

Importantly, the activation of **NF**-**kB** in vascular endothelial cells by diverse signals can be specifically inhibited by antioxidants such as N-acetylcysteine and pyrrolidine dithiocarbamate (see. . . 07/969,934, now allowed). This has led to the hypothesis that oxygen radicals play an important role in the activation of **NF**-**kB** through an undefined oxidation-reduction mechanism. Because an **NF**-**kB**-like enhancer element also regulates the transcription of the VCAM-1 promoter in an oxidation-reduction-sensitive manner, oxidative stress in the atherosclerotic lesion. . .

DRAWING DESC:

DRWD(8)

FIG. . . . an illustration of an autoradiogram that indicates that linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. HAEC were split at the ratio to give approximately 60% confluence in 100-mm tissue culture plates. HAEC were. . .

DRAWING DESC:

DRWD(9)

FIG. 8 is an illustration of an acrylamide gel slab that indicates that polyunsaturated fatty acids activate **NF**-**kB**-like DNA binding activities that are blocked by the antioxidant PDTC. Confluent HAEC in media containing 4% FBS (as described in. . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(31)

Previous . . . promoter studies that cytokines and non-cytokines activate VCAM-1 gene expression in endothelial cells at least in part transcriptionally through two **NF**-**kB**-like DNA binding elements. It has also been demonstrated that PDTC inhibits VCAM-1 gene expression through a redox-sensitive **NF**-**kB** like factor. To determine whether

polyunsaturated fatty acids induce transcriptional activation of the human VCAM-1 promoter via a similar mechanism,. . . results were obtained with the minimal cytokine-inducible promoter of the VCAM-1 gene (p85 VCAM-CAT), containing the -77 and -63 bp **NF**-**kB**-like sites. Neither linoleic acid nor TNF-.alpha. had any effect on activity using a constitutively expressed pSV.sub.2 CAT construct. PDTC inhibited. . . indicate that analogous to TNF-.alpha., polyunsaturated fatty acids such as linoleic acid induce the transcriptional activation of VCAM-1 through an **NF**-**kB**-like redox-sensitive mechanism.

DETDESC:

DETD(32)

To determine whether polyunsaturated fatty acids and their oxidative metabolites regulate VCAM-1 promoter activity through an **NF**-**kB**-like transcriptional regulatory factor, nuclear extracts from HAEC were assayed for DNA binding activity to a double-stranded oligonucleotide containing the VCAM-1 **NF**-**kB**-like promoter elements located at positions -77 and -63. As shown in FIG. 7, two bands A and C, representing **NF**-**kB**-like activity were induced in response to a three hour exposure to linoleic acid (7.5 .mu.M). Similar findings were observed on. . . exposure to the cytokine TNF-.alpha. (100 U/ml). A weak band B was observed in control (untreated) cells. No induction of **NF**-**kB**-like binding was observed with the monounsaturated fatty acid oleic acid. Pretreatment of the cells for thirty minutes with PDTC inhibited. . . previously reported findings that PDTC blocks the activation of VCAM-1 gene expression in HUVEC by inhibiting the activation of these **NF** **KB**-like DNA binding proteins.

DETDESC:

DETD(57)

FIG. 7 illustrates the results of this experiment. Linoleic acid induces transcriptional activation of the VCAM-1 promoter by a redox-sensitive **NF**-**kB** like factor. These results are similar to those observed by the activation of VCAM-1 promotor by cytokines such as TNF-.alpha.... .

DETDESC:

DETD(59)

Polyunsaturated Fatty Acids Activate **NF**-**kB**-like DNA Binding Activities that are Blocked by the Antioxidant PDTC

DETDESC:

DETD(60)

Confluent . . . native acrylamide gels, and exposed to autoradiography film at -70.degree. C. for 18 hours. Two bands A and C, representing **NF**-**kB** like binding activity are designated. A weak band B was observed in control (untreated) cells.

DETDESC:

DETD(61)

FIG. 8 illustrates that linoleic acid induces **NF**-**kB** binding activity to VCAM-1 promotor in a redox-sensitive manner. This is analogous to cytokine TNF-.alpha. and suggests a similar mechanism. . .

US PAT NO: 5,747,471 [IMAGE AVAILABLE] L15: 38 of 72
DATE ISSUED: May 5, 1998
TITLE: Cationic amphiphiles containing steroid lipophilic groups for intracellular delivery of therapeutic molecules
INVENTOR: Craig S. Siegel, Woburn, MA
David J. Harris, Lexington, MA
Edward R. Lee, Quincy, MA
Shirley C. Hubbard, Belmont, MA
Seng H. Cheng, Wellesley, MA
Simon J. Eastman, Marlboro, MA
John Marshall, Milford, MA
Ronald K. Scheule, Hopkinton, MA
Mathieu B. Lane, Cambridge, MA
Eric A. Rowe, Malden, MA
ASSIGNEE: Genzyme Corporation, Cambridge, MA (U.S. corp.)
APPL-NO: 08/540,867
DATE FILED: Oct. 11, 1995
ART-UNIT: 184
PRIM-EXMR: Jacqueline M. Stone
ASST-EXMR: Patrick Twomey
LEGAL-REP: E. Victor Donahue

US PAT NO: 5,747,471 [IMAGE AVAILABLE] L15: 38 of 72
US-CL-CURRENT: **514/44**, **182**, **777**; 552/544; 560/6

DETDESC:

DETD(296)

It . . . that increase with the severity of an inflammatory condition (for example, tumor necrosis factor "TNF", and transcription factors such as **NF**-**kB**, AP-1, NF-IL6 and octamer binding protein). It has also been determined that interleukin 8, a polypeptide of 8,500 MW, is. . .

US PAT NO: 5,744,131 [IMAGE AVAILABLE] L15: 39 of 72
DATE ISSUED: Apr. 28, 1998
TITLE: Sequence-directed DNA-binding molecules compositions and methods
INVENTOR: Cynthia A. Edwards, Menlo Park, CA
Kirk E. Fry, Palo Alto, CA
Charles R. Cantor, Boston, MA
Beth M. Andrews, Maynard, MA
ASSIGNEE: Genelabs Technologies, Inc., Redwood City, CA (U.S. corp.)
APPL-NO: 08/476,876
DATE FILED: Jun. 7, 1995
ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
ASST-EXMR: Amy Atzel
LEGAL-REP: Gary R. Fabian, Carol A. Stratford, Peter J. Dehlinger

US PAT NO: 5,744,131 [IMAGE AVAILABLE] L15: 39 of 72
US-CL-CURRENT: 424/78.08; 436/501; **514/1**

DETDESC:

DETD(219)

Similarly, . . . nuclear factor (HNF-1), which is required for the expression of human hepatitis B virus (HBV) (Chang, H. -K.), and (ii) **NFkB** and NFAT-1 binding sites in the human immunodeficiency virus (HIV) long terminal repeat (LTR), one or both of which may. . .

DETDESC:

DETD(222)
. . .
of
E2 genital warts,
replication cervical carcinoma
Interleukin 2
NFAT-1 immunosuppressant
enhancer
HIV LTR NFAT-1 AIDS, ARC
NFkB
HBV enhancer
HNF-1 hepatitis
Fibrogen promoter
HNF-1 cardiovascular
disease
Oncogene promoter
?? cancer
and coding sequences. . .

DETDESC:

DETD(223)
(Abbreviations: . . . virus; HPV, human papilloma virus; HIV LTR, Human immunodeficiency virus long terminal repeat; NFAT, nuclear factor of activated T cells; **NFkB**, nuclear factor kappaB; AIDS, acquired immune deficiency syndrome; ARC, AIDS related complex; HBV, hepatitis **B** virus; HNF, hepatic **nuclear** **factor**.)

US PAT NO: 5,738,852 [IMAGE AVAILABLE] L15: 40 of 72
DATE ISSUED: Apr. 14, 1998
TITLE: Methods of enhancing antigen-specific T cell responses
INVENTOR: William S. Robinson, Palo Alto, CA
Keting Chu, Palo Alto, CA
ASSIGNEE: Solis Therapeutics, Inc., Palo Alto, CA (U.S. corp.)
APPL-NO: 08/663,157
DATE FILED: Jul. 29, 1996
ART-UNIT: 185
PRIM-EXMR: Johnny F. Railey, II
LEGAL-REP: Pennie & Edmonds LLP

US PAT NO: 5,738,852 [IMAGE AVAILABLE] L15: 40 of 72
US-CL-CURRENT: 424/199.1, 93.2, 278.1; 435/320.1; **514/44**

DETDESC:

DETD(37)

In . . . be inserted upstream of the transcriptional control regions.

Alternatively, or in addition, multimeric transcription factor binding sites (e.g., NF-AT and/or **NFKB**) may be inserted into or upstream of the transcriptional control regions, combining the upstream region of one with the proximal. . .

US PAT NO: 5,736,570 [IMAGE AVAILABLE] L15: 41 of 72
DATE ISSUED: Apr. 7, 1998
TITLE: Immunotherapeutic aryl amides
INVENTOR: George W. Muller, Bridgewater, NJ
Mary Shire, North Plainfield, NJ
David I. Stirling, Branchburg, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/729,847
DATE FILED: Oct. 15, 1996
ART-UNIT: 123
PRIM-EXMR: Jane Fan
LEGAL-REP: Mathews, Collins, Shepherd & Gould

US PAT NO: 5,736,570 [IMAGE AVAILABLE] L15: 41 of 72
US-CL-CURRENT: **514/532**, **535**, **617**, **619**, **622**

SUMMARY:

BSUM(14)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,733,762 [IMAGE AVAILABLE] L15: 42 of 72
DATE ISSUED: Mar. 31, 1998
TITLE: Complexes of nucleic acid and polymer, their process of preparation and their use for the transfection of cells
INVENTOR: Patrick Midoux, Orleans, France
Patrick Erbacher, Orleans, France
Annie-Claude Roche-Degremont, Sandillon, France
Michel Monsigny, Saint-Cyr-En-Val, France
ASSIGNEE: I.D.M. Immuno-Designed Molecules, France (foreign corp.)
APPL-NO: 08/741,678
DATE FILED: Oct. 31, 1996
ART-UNIT: 189
PRIM-EXMR: George C. Elliott
ASST-EXMR: Thomas G. Larson
LEGAL-REP: Bierman, Muserlian and Lucas

US PAT NO: 5,733,762 [IMAGE AVAILABLE] L15: 42 of 72
US-CL-CURRENT: 435/458, 325; **514/44**; 530/300, 345, 350, 395, 402; 536/23.2, 23.5, 23.7, 24.5

SUMMARY:

BSUM(146)
nuclear factors: **NF**-**KB**, CII TA, . . .

US PAT NO: 5,723,335 [IMAGE AVAILABLE] L15: 43 of 72
DATE ISSUED: Mar. 3, 1998
TITLE: Immune stimulation by phosphorothioate oligonucleotide analogs
INVENTOR: Stephen L. Hutcherson, Richmond, VA
Josephine M. Glover, Woking, United Kingdom
ASSIGNEE: Isis Pharmaceuticals, Inc., Carlsbad, CA (U.S. corp.)
APPL-NO: 08/712,135
DATE FILED: Sep. 11, 1996
ART-UNIT: 189
PRIM-EXMR: Charles C.P. Rories
LEGAL-REP: Law Offices of Jane Massey Licata

US PAT NO: 5,723,335 [IMAGE AVAILABLE] L15: 43 of 72
US-CL-CURRENT: 435/375; 424/1.73, 1.77, 280.1; **514/44**; 536/23.1, 24.3, 24.31, 24.33

SUMMARY:

BSUM(18)

Oligonucleotides having a sequence identical to a portion of the sense strand of the mRNA encoding the p65 subunit of **NF**-**kB**, a DNA binding protein, were found to stimulate splenic cell proliferation both in vitro and in vivo. The proliferating spleen cells were shown to be B cells. Immunoglobulin secretion and **NF**-**kB** activity in these cell lines was also increased by the sense oligonucleotide. Both phosphodiester and phosphorothioate sense oligonucleotides stimulated the. . .

US PAT NO: 5,719,131 [IMAGE AVAILABLE] L15: 44 of 72

DATE ISSUED: Feb. 17, 1998
TITLE: Cationic amphiphiles containing dialkylamine lipophilic groups for intracellular delivery of therapeutic molecules
INVENTOR: David J. Harris, Lexington, MA
Edward R. Lee, Quincy, MA
Craig S. Siegel, Woburn, MA
Seng H. Cheng, Wellesley, MA
Simon J. Eastman, Marlboro, MA
John Marshall, Milford, MA
Ronald K. Scheule, Hopkinton, MA
ASSIGNEE: Genzyme Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/546,110
DATE FILED: Oct. 20, 1995
ART-UNIT: 184
PRIM-EXMR: Christopher S.F. Low
ASST-EXMR: Dave T. Nguyen

US PAT NO: 5,719,131 [IMAGE AVAILABLE] L15: 44 of 72
US-CL-CURRENT: **514/44**; 424/450; 552/544

DETDESC:

DETD(297)

It . . . increase with the severity of an inflammatory condition (for example, tumor necrosis factor "TNF" and potentially transcription factors such as **NF**-**kB**, AP-1, NF-IL6 and octamer binding protein). It has also been determined that interleukin 8, a polypeptide of 8,500 MW, is. . .

US PAT NO: 5,703,098 [IMAGE AVAILABLE] L15: 45 of 72
DATE ISSUED: Dec. 30, 1997
TITLE: Immunotherapeutic imides/amides
INVENTOR: George W. Muller, Bridgewater, NJ
Mary Shire, North Plainfield, NJ
David I. Stirling, Branchburg, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/759,788
DATE FILED: Dec. 3, 1996
ART-UNIT: 121
PRIM-EXMR: Floyd D. Higel
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,703,098 [IMAGE AVAILABLE] L15: 45 of 72
US-CL-CURRENT: **514/339**, **417**; 546/277.1; 548/476

SUMMARY:

BSUM(14)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,703,069 [IMAGE AVAILABLE] L15: 46 of 72
DATE ISSUED: Dec. 30, 1997
TITLE: Method for inhibiting and controlling viral growth
INVENTOR: David Thomas Connor, Ann Arbor, MI
Stephen Joseph Gracheck, Ann Arbor, MI
ASSIGNEE: Warner-Lambert Company, Morris Plains, NJ (U.S. corp.)
APPL-NO: 08/712,063
DATE FILED: Sep. 11, 1996
ART-UNIT: 122
PRIM-EXMR: Robert T. Bond
LEGAL-REP: Charles W. Ashbrook

US PAT NO: 5,703,069 [IMAGE AVAILABLE] L15: 46 of 72
US-CL-CURRENT: **514/211**, **220**; 540/488, 495

SUMMARY:

BSUM(7)

An . . . further development is therapeutic targeting along cellular signaling pathways that result in HIV-1 transcriptional activation. Among the potential targets is **nuclear** **factor**-.**kappa**.**B** (NF-.**kappa**.B), a transcriptional enhancer important for HIV-1 activation. In resting cells, preformed NF-.kappa.B exists in the cytoplasm bound to its inhibitor. . .

US PAT NO: 5,698,579 [IMAGE AVAILABLE] L15: 47 of 72
DATE ISSUED: Dec. 16, 1997
TITLE: Cyclic amides
INVENTOR: George W. Muller, Bridgewater, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)

APPL-NO: 08/703,708
DATE FILED: Aug. 27, 1996
ART-UNIT: 123
PRIM-EXMR: Alan L. Rotman
ASST-EXMR: D. Margaret M. Mach
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,698,579 [IMAGE AVAILABLE] L15: 47 of 72
US-CL-CURRENT: **514/416**; 548/512

SUMMARY:

BSUM(12)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,691,338 [IMAGE AVAILABLE] L15: 48 of 72
DATE ISSUED: Nov. 25, 1997
TITLE: 1,2-dithiole-3 thiones for the treatment of reverse transcriptase-dependent viral infections
INVENTOR: Hans J. Prochaska, New York, NY
Bruce Polsky, New York, NY
ASSIGNEE: Sloan-Kettering Institute for Cancer Research, New York, NY (U.S. corp.)
APPL-NO: 08/485,658
DATE FILED: Jun. 7, 1995
ART-UNIT: 124
PRIM-EXMR: Samuel Barts
LEGAL-REP: John P. White

US PAT NO: 5,691,338 [IMAGE AVAILABLE] L15: 48 of 72
US-CL-CURRENT: **514/252**, **262**, **274**, **441**

SUMMARY:

BSUM(5)

This . . . by which these thiols inhibit HIV-1 replication is believed to be due to their ability to inhibit the activation of **Nuclear** **Factor** .**kappa**.**B** under conditions of oxidative stress (7). There has been enthusiasm for testing compounds such as N-acetylcysteine or the ester of. . .

DETDESC:

DETD(59)
7. Staal F. J., M. Roederer, and L. A. Herzenberg. Intracellular thiols regulate activation of **nuclear** **factor** **kappa** **B** and transcription of human immunodeficiency virus. Proc. Natl. Acad. Sci. 87:9943-9947 (1990).

US PAT NO: 5,686,436 [IMAGE AVAILABLE] L15: 49 of 72
DATE ISSUED: Nov. 11, 1997
TITLE: Multi-faceted method to repress reproduction of latent viruses in humans and animals
INVENTOR: Knox Van Dyke, Morgantown, WV
ASSIGNEE: HIV Diagnostics, Inc., Lexington, KY (U.S. corp.)
APPL-NO: 08/317,730
DATE FILED: Oct. 4, 1994
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Price, Heneveld, Cooper, DeWitt & Litton

US PAT NO: 5,686,436 [IMAGE AVAILABLE] L15: 49 of 72
US-CL-CURRENT: **514/171**, **198**, **369**, **374**, **378**, **561**, **563**

ABSTRACT:
Disclosed . . . such as HIV, in animals by the generally concurrent administration of (1) antioxidants including a glutathione agent; and (2) an **NFKB** induction inhibitor. Also disclosed are pharmaceutical compositions and kits for use in repressing reproduction of latent viruses such as HIV.

SUMMARY:

BSUM(8)

Schreck . . . The iKB factor is removed from the protein triad and the remaining p50, p65 complex becomes known as NF-kappa B (**NFKB**).

SUMMARY:

BSUM(9)

Schreck et al. have recognized that **NFKB** is a gene transcription factor that migrates into the nucleus of the HIV infected cell and switches on the production. . . expression of HIV-1 in a human T cell line. They further report that the expression of HIV is mediated by **NFKB** transcription factor which is potently and rapidly activated by a hydrogen peroxide treatment of cells from its inactive cytoplasmic form. They additionally report that N-acetyl cysteine and other thiol compounds block the activation of **NFKB**. They concluded that these diverse agents thought to activate **NFKB** by distinct intracellular pathways might act through a common mechanism involving the synthesis of reactive oxygen intermediates. They did not. . .

SUMMARY:

BSUM(10)

Sherman et al., Biochem. Biophys. Res. Comm., 191 (3):1301-1308, 1993, report that pyrrolidine dithiocarbamate (PDTC) is an inhibitor of **NFKB** activation. They further report that this compound is an inhibitor of nitric oxide synthase (NO synthase). They further report that. . . that PDTC may act as a scavenger of reactive oxygen species which prevents them from participation in the activation of **NFKB**.

SUMMARY:

BSUM(15)

The . . . the generally concurrent administration of 1) a glutathione agent; 2) at least one additional antioxidant; and 3) at least one **NFKB** induction inhibitor. Further aspects and advantages of the invention will be apparent to those skilled in the art upon review. . .

DETDESC:

DETD(3)

There . . . glutathione precursor, a glutathione production enhancer, or glutathione, (2) high doses of additional fat- and water-soluble antioxidants, and (3) an **NFKB** induction inhibitor, to an animal infected with a latent virus. The fat- and water-soluble antioxidants are administered to an animal. . .

DETDESC:

DETD(5)

The Role of **NFKB** and Peroxynitrite in the Activation of a Cell to Reproduce HIV

DETDESC:

DETD(6)

NFKB is a gene transcription factor that switches on the production of the HIV virus of a vitally infected cell. **NFKB** is known to activate a variety of genes, including the transcription of a variety of cytokines, viruses and NO Synthase.. . .

DETDESC:

DETD(10)

Peroxynitrite is significant in that it activates **NFKB**. **NFKB** is inactivated by I Kappa B (IKB) which acts on **NFKB** via the P65 subunit. As shown in FIG. 1, peroxynitrite cleaves IKB, thereby releasing the active **NFKB**.

DETDESC:

DETD(28)

NFKB Induction Inhibitors

DETDESC:

DETD(29)

NFKB induction inhibitors are agents that inhibit **NFKB** transcription factor from binding to DNA. This blocks the induction of HIV or other viral reproduction by directly suppressing the vital reproduction activating mechanism. **NFKB** inhibitors (item 7, FIG. 2) also suppress peroxynitrite synthesis, by preventing **NFKB** from activating cell genes to produce NO synthase.

DETDESC:

DETD(32)

The preferred type of **NFKB** induction inhibitor is an anti-inflammatory steroid. Examples of suitable anti-inflammatory

steroids suitable as **NFKB** induction inhibitors include but are not limited to predonsone, prednisolone, methyl prednisolone, dexamethasone, beta metasone dehydroepiandrosterone, 9a-fluorocortisol, prednisone, aetiocholanolone, 2-methylcortisol, pregnanediol, deoxycorticosterone, cortisone, hydrocortisone (cortisol), 6a-methylprednisolone, triamcinolone, estrogen or derivatives thereof. Generally, any steroid with antiinflammatory action toward **NFKB** may be used. In addition, one or more suitable nonglucocorticoid lazaroids may be utilized as **NFKB** induction inhibitors. Preferred lazaroids include, but are not limited to, U-74006F, which is 21-[4-(2,6-di-1-pyrrolidinyl-4-pyrimidinyt)-1-piperazinyl]-16-methyl-(16.alpha.)-pregna-1,4,9(11)-triene-3,20-dione monomethanesulfonate or TIRILAZAD mesylate or. . .

DETDESC:

DETD(36)
In . . . Other antiinflammatory steroids can be substituted at appropriate doses, as set forth in the Physicians' Desk Reference. Adminstration of an **NFKB** induction inhibitor such as an anti-inflammatory steroid, is one of the most important steps in the treatment of HIV, AIDS. . .

DETDESC:

DETD(39)

In addition, to the previously noted anti-inflammatory steroids and lazaroids, a variety of other compounds may be utilized as **NFKB** induction inhibitors such as pyrrolidine dithiocarbamate and other dithiocarbamates, and glycyrrhizic acid (from licorice root). A preferred dosage level when. . . is about 100 mg/day per person for each day of therapy. In addition, other compounds are suitable for use as **NFKB** induction inhibitors. These inhibitors include, but are not limited to, immunosuppressants such as cyclosporin A, rapamycin, interleukin 10, and FK. . . Clearly, a wide array of plant steroids, male steroids, female steroids, glucocorticoids, lazaroids, and 21-aminosteroids are eligible for use as **NFKB** induction inhibitors.

DETDESC:

DETD(40)

An inhibitor known to be effective against **NFKB** binding or expressing is mevinolin, a drug which prevents isoprenylation and methylthioadenosine (MTA) and inhibitor of several S adenosylmethionine dependent. . .

DETDESC:

DETD(47)

Although . . . antioxidants, glutathione agents, and steroids with regard to HIV production. HIV replication is blocked by a combination of antioxidants and **NFKB** induction inhibitor. About 70% of the blocking action of HIV replication is believed to stem from the **NFKB** induction inhibitor, which preferably is one or more anti-inflammatory steroids. Although such steroids do not have direct inhibitory activity, they control viral synthesis by blocking **NFKB** induction. As will be recalled, **NFKB** is a DNA transcription factor made of protein. **NFKB** controls a whole series of inflammatory cytokines and NO synthase as well as HIV and FIV replication. Upon introduction of. . .

DETDESC:

DETD(48)

However, for **NFKB** to be active it must shed its inhibitory factor I kappa B. Such shedding requires oxidation because the bonds holding. . . to proteins P50 and P65 are sensitive to oxidation. Thus, antioxidants keep the I kappa B inhibitory factor bound to **NFKB** and therefore inactive.. The role of antioxidants in the mechanism depicted in FIG. 3 is believed to be responsible for about 30% of the activity of producing **NFKB**, and preventing HIV replication.

DETDESC:

DETD(49)

All . . . known to those skilled in the art. Although it is most preferred to administer the anitoxidants including glutathione agent and **NFKB** induction inhibitor concurrently, or simultaneously, it is not a requirement. Thus, the preferred embodiments of the present invention also encompass. . .

DETDESC:

DETD(51)

The . . . a glutathione agent; (2) an effective amount of one or more additional antioxidants; and (3) an effective amount of an **NFKB** induction inhibitor. In a most preferred embodiment, the pharmaceutical compositions comprise: (1) an effective amount of a glutathione agent, e.g.. . . antioxidant, (2b) an effective amount of a fat-soluble antioxidant, and (3) an effective amount of an anti-inflammatory steroid as the **NFKB** induction inhibitor. The other ingredients described above may also be included.

DETDESC:

DETD(58)

In . . . C, A and E; an effective amount of at least one glutathione precursor such as N-acetyl cysteine; followed by an **NFKB** induction inhibitor such as one or more anti-inflammatory steroids or lazaroids. As summarized in Table 4 below, seven cats heavily. . . 10 to about 18 pounds. The cats were initially treated with a single dosage of an effective amount of an **NFKB** induction inhibitor, that is an antiinflammatory steroid dose of DEPO-MEDROL (20-25 mg) and a series of oral dosages of a. . .

DETDESC:

DETD(62)

In . . . fat-soluble antioxidants and an effective amount of at least one glutathione precursor such as N-acetyl cysteine are administered. Before an **NFKB** induction inhibitor is administered, the CD.sub.4 (T-lymphocyte) count is increased to about 100 cells/mm.sup.3 or more. The CD.sub.4 count may. . . concentrates containing monocytes may be given, such as via transfusions. Once CD.sub.4 counts are about 100 cells/mm.sup.3 or more, an **NFKB** induction inhibitor is administered.

DETDESC:

DETD(63)

In both the preferred and optional treatment regimens, the **NFKB** induction inhibitor is administered until AIDS(-) is indicated from AIDS(+) blood assay, via ELISA Western blot, and PCR (polymerase chain. . .

DETDESC:

DETD(74)

Preferably, . . . suitable glutathione precursors could be utilized in place of, or instead of the N-acetyl cysteine. Similarly, one or more other **NFKB** induction inhibitors could be utilized in place of or instead of the methyl prednisolone.

DETDESC:

DETD(77)

The . . . one fat soluble antioxidant at doses higher than the recommended daily minimum requirements, and preferably, only slight amounts or no **NFKB** induction inhibitor. In a most preferred treatment regimen, the subject suffering from symptoms of the Herpes virus is administered generally. . .

CLAIMS:

CLMS(1)

The . . .

for suppressing the reproduction of human immunodeficiency virus in a human, comprising administering to such human:
(i) at least one **NFKB** induction inhibitor in an amount effective to inhibit **nuclear** **factor** **kappa** **B**; said at least one **NFKB** induction inhibitor being selected from the group consisting of anti-inflammatory steroids and nonglucocorticoid lazaroids;
(ii) at least one fat-soluble antioxidant at. . .

CLAIMS:

CLMS(13)

13. The method of claim 1 wherein said **NFKB** induction inhibitor comprises an anti-inflammatory steroid.

CLAIMS:

CLMS(14)

14. . . . 1 further comprising administering to such human:
(v) an effective amount of a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

CLAIMS:

CLMS(15)

15. . . . suppressing the reproduction of feline immunodeficiency virus and/or feline leukemia virus, comprising administering to a cat: (i) at least one **NFKB** induction inhibitor in art amount effective to inhibit **nuclear** **factor** **kappa** **B**; said at least one **NFKB** induction inhibitor being selected from the group consisting of anti-inflammatory steroids and nonglucocorticoid lazaroids; (ii) at least one fat-soluble antioxidant at. . .

CLAIMS:

CLMS(20)

20. The method of claim 15 wherein said **NFKB** induction inhibitor comprises an anti-inflammatory steroid.

CLAIMS:

CLMS(21)

21. . . . 15 further comprising administering to such cat: (v) an effective amount of a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

CLAIMS:

CLMS(26)

26. . . . 24 further comprising administering to such animal: (v) an effective mount of a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

CLAIMS:

CLMS(30)

30. . . . 28 further comprising administering to such animal; (v) an effective mount of a peroxynitrite production suppressor in addition to said **NFKB** induction inhibitor.

US PAT NO: 5,683,987 [IMAGE AVAILABLE] L15: 50 of 72
DATE ISSUED: Nov. 4, 1997
TITLE: Therapeutic oligonucleotides targeting the human MDR1 and MRP genes
INVENTOR: Larry J. Smith, Omaha, NE
ASSIGNEE: The Board of Regents of the University of Nebraska, Lincoln, NE (U.S. corp.)
APPL-NO: 08/487,141
DATE FILED: Jun. 7, 1995
ART-UNIT: 189
PRIM-EXMR: George G. Elliott
ASST-EXMR: Andrew Wang
LEGAL-REP: Dann, Dorfman, Herrell and Skillman

US PAT NO: 5,683,987 [IMAGE AVAILABLE] L15: 50 of 72
US-CL-CURRENT: **514/44**; 536/23.1, 24.31, 24.5

SUMMARY:

BSUM(10)

In . . . transplant models (Kitajima et al., J. Biol. Chem. 267:25881-25888, 1992). Others have targeted genes in cancer cells, including c-myc, c-Ha-ras, **NF**-**kB**, c-myb, c-kit and bcr-abl. In each of these instances involving the administration of ODNs to treat animals with xenogeneic human. . .

DETDESC:

DETD(62)
. . .
556 22 cap site
+
LOW(3)mdr 11 20 low Tm +
Cohen(1)mdr
86 1130 15 published
+
NF-**kB**(1)mdr 296 22 3; TR --
binding
CAT(L)mdr 432 20 TR binding
--
Y-box-mdr 464 22 TR binding
. . .

US PAT NO: 5,679,684 [IMAGE AVAILABLE] L15: 51 of 72
DATE ISSUED: Oct. 21, 1997
TITLE: Hydroxyalkylammonium-pyrimidines and nucleoside derivatives, useful as inhibitors of inflammatory cytokines
INVENTOR: Bradley J. Benson, Chapel Hill, NC
Xiannong Chen, Athens, GA
George J. Cianciolo, Chapel Hill, NC
Jose-Luis Diaz, Durham, NC
Khalid S. Ishaq, Chapel Hill, NC
Susan L. Morris-Natschke, Apex, NC
Ronald J. Uhing, Durham, NC
Henry Wong, Morrisville, NC
ASSIGNEE: Macronex, Inc., Morrisville, NC (U.S. corp.)
The University of N.C. at Chapel Hill, Morrisville, NC (U.S. corp.)
APPL-NO: 08/476,704
DATE FILED: Jun. 7, 1995
ART-UNIT: 122
PRIM-EXMR: Yogendra N. Gupta
LEGAL-REP: Klauber & Jackson

US PAT NO: 5,679,684 [IMAGE AVAILABLE] L15: 51 of 72
US-CL-CURRENT: **514/269**, **50**, **274**

SUMMARY:

BSUM(3)

Two . . . that they employ different signal transduction pathways. While both receptors are capable of binding TNF and activating the transcription factor **NFkB**, it appears that the expression of each receptor is independently and differentially regulated. Human TNF-.alpha. will bind to both types. . .

US PAT NO: 5,663,153 [IMAGE AVAILABLE] L15: 52 of 72
DATE ISSUED: Sep. 2, 1997
TITLE: Immune stimulation by phosphorothioate oligonucleotide analogs
INVENTOR: Stephen L. Hutcherson, Richmond, VA
Josephine M. Glover, Woking, United Kingdom
ASSIGNEE: Isis Pharmaceuticals, Inc., Carlsbad, CA (U.S. corp.)
APPL-NO: 08/467,930
DATE FILED: Jun. 6, 1995
ART-UNIT: 189
PRIM-EXMR: Charles C.P. Rories
LEGAL-REP: Law Offices of Jane Massey Licata

US PAT NO: 5,663,153 [IMAGE AVAILABLE] L15: 52 of 72
US-CL-CURRENT: **514/44**; 424/1.11, 1.73, 1.77, 278.1, 280.1; 536/23.1, 24.5

SUMMARY:

BSUM(18)

Oligonucleotides having a sequence identical to a portion of the sense strand of the mRNA encoding the p65 subunit of **NF**-**kB**, a DNA binding protein, were found to stimulate splenic cell proliferation both in vitro and in vivo. The proliferating spleen cells were shown to be B cells. Immunoglobulin secretion and **NF**-**kB** activity in these cell lines was also increased by the sense oligonucleotide. Both phosphodiester and phosphorothioate sense oligonucleotides stimulated the. . .

US PAT NO: 5,658,940 [IMAGE AVAILABLE] L15: 53 of 72
DATE ISSUED: Aug. 19, 1997
TITLE: Succinimide and maleimide cytokine inhibitors
INVENTOR: George W. Muller, Bridgewater, NJ
Mary Shire, North Plainfield, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/539,879
DATE FILED: Oct. 6, 1995
ART-UNIT: 121
PRIM-EXMR: Jacqueline Haley
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,658,940 [IMAGE AVAILABLE] L15: 53 of 72
US-CL-CURRENT: **514/417**, **309**, **339**, **340**, **421**, **425**; 546/142, 277.1, 278.4, 278.7; 548/465, 479, 513, 547

SUMMARY:

BSUM(14)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,650,316 [IMAGE AVAILABLE] L15: 54 of 72
DATE ISSUED: Jul. 22, 1997
TITLE: Uses of triplex forming oligonucleotides for the treatment of human diseases
INVENTOR: Bharat B. Aggarwal, Houston, TX
Robert F. Rando, The Woodlands, TX
Michael E. Hogan, The Woodlands, TX
ASSIGNEE: Research Development Foundation, Carson City, NV (U.S. corp.)
APPL-NO: 08/254,114
DATE FILED: Jun. 6, 1994
ART-UNIT: 189
PRIM-EXMR: Charles C. P. Rories
LEGAL-REP: Benjamin Aaron Adler

US PAT NO: 5,650,316 [IMAGE AVAILABLE] L15: 54 of 72
US-CL-CURRENT: 435/375, 6, 7.23; **514/44**; 536/24.31, 24.32, 24.33, 24.5

DRAWING DESC:

DRWD(11)

FIG. 9 shows the antiproliferative effects of the TFOs J111-50 (Intron 3) and J109-50 (**NF**-**kB**) on a human glioblastoma (U-251) cell line.

DETDESC:

DETD(9)

. . .

990	cholesterol scramble sequence of J111-51
B106-96	phosphorothioate G-rich TFO
1208	phosphorothioate random
J109-51	cholesterol TNF (**NF**-**kB**); -237 to -238

DETDESC:

DETD(53)

FIGS. 9, top and bottom the antiproliferative effects of the TFOs J111-50 (Intron 3) and J109-50 (**NF**-**kB**) on a human glioblastoma (U-251) cell line, respectively. Both J111-50 (directed to Intron 3) and J109-50 (directed to **NF**-**kB**) inhibited the growth of U-251 cells by about 80% at approximately 1 .mu.M.

DETDESC:

DETD(63)

Table . . . untreated cells was expressed as 100%. All determinations were made in triplicate. TFO 109-50, 111-51, 108-56 and 108-57 are from **NF**-**kB** (-237 to -208); Intron 3 (+1429 to +1456); and SP-1 (-58 to -33) sites respectively. J109-50 had amino group whereas. . .

US PAT NO: 5,646,185 [IMAGE AVAILABLE] L15: 55 of 72
DATE ISSUED: Jul. 8, 1997
TITLE: Tumor treatment method
INVENTOR: Amato J. Giaccia, Stanford, CA
Albert C. Koong, Palo Alto, CA
ASSIGNEE: The Board of Trustees of the Leland Stanford Junior University, Stanford, CA (U.S. corp.)
APPL-NO: 08/137,238
DATE FILED: Oct. 14, 1993
ART-UNIT: 124
PRIM-EXMR: Paul J. Killos
LEGAL-REP: Susan T. Evans, Carol A. Stratford, Peter J. Dehlinger

US PAT NO: 5,646,185 [IMAGE AVAILABLE] L15: 55 of 72
US-CL-CURRENT: **514/548**

DRAWING DESC:

DRWD(10)

FIG. 6B shows sequences of PKC responsive elements **NFKB** (SEQ ID NO: 2), HSE (SEQ ID NO: 3), GRE SEQ ID NO: 4 and AP1-1 (SEQ ID NO: 5). . .

DETDESC:

DETD(61)

As . . . upstream of the TNF gene. Exemplary PKC Responsive elements that may be included in the vector include Glucose-related Core element, **Nuclear** **Factor**-**kappa** **B** (**NFKB**), Heat shock transcription factor (HSE), GRE and AP-1. Sequences for these exemplary elements are shown in FIG. 6B. Inclusion of. . .

US PAT NO: 5,643,893 [IMAGE AVAILABLE] L15: 56 of 72
DATE ISSUED: Jul. 1, 1997
TITLE: N-substituted-(Dihydroxyboryl)alkyl purine, indole and pyrimidine derivatives, useful as inhibitors of inflammatory cytokines
INVENTOR: Bradley J. Benson, Chapel Hill, NC
Xiannong Chen, Athens, GA
George J. Cianciolo, Chapel Hill, NC
Jose-Luis Diaz, Durham, NC
Khalid S. Ishaq, Chapel Hill, NC
Susan L. Morris-Natschke, Apex, NC
Ronald J. Uhing, Durham, NC
Henry Wong, Morrisville, NC
ASSIGNEE: Macronex, Inc., Wayne, PA (U.S. corp.)
University of North Carolina, Chapel Hill, NC (U.S. corp.)
APPL-NO: 08/264,039
DATE FILED: Jun. 22, 1994
ART-UNIT: 122
PRIM-EXMR: Emily Bernhardt
LEGAL-REP: Klauber & Jackson

US PAT NO: 5,643,893 [IMAGE AVAILABLE] L15: 56 of 72
US-CL-CURRENT: **514/64**; 544/229; 548/405; 562/7

SUMMARY:

BSUM(3)

Two . . . that they employ different signal transduction pathways. While both receptors are capable of binding TNF and activating the transcription factor **NFkB**, it appears that the expression of each receptor is independently and differentially regulated. Human TNF-.alpha. will bind to both types. . .

US PAT NO: 5,641,773 [IMAGE AVAILABLE] L15: 57 of 72
DATE ISSUED: Jun. 24, 1997
TITLE: Methods for treating viral infections
INVENTOR: Arthur P. Pardee, Brookline, MA
Debajit K. Biswas, Newton, MA
Bruce J. Dezube, Newton Centre, MA
ASSIGNEE: Dana-Farber Cancer Institute, Boston, MA (U.S. corp.)
APPL-NO: 08/159,509
DATE FILED: Nov. 30, 1993
ART-UNIT: 129
PRIM-EXMR: Brian M. Burn
LEGAL-REP: David G. Conlin, Ronald I. Eisenstein

US PAT NO: 5,641,773 [IMAGE AVAILABLE] L15: 57 of 72
US-CL-CURRENT: **514/221**, **258**, **262**, **264**

DETDESC:

DETD(4)

Mapping . . . in trans-activating (stimulating) viral gene expression by interaction with the tar element which is present in this region. Similarly, the **nuclear** **factor** NF-.**kappa**.**B** can also stimulate viral gene expression through its interaction with sequences present in the LTR [Sen, R., et al, Cell. . .

US PAT NO: 5,635,517 [IMAGE AVAILABLE] L15: 58 of 72
DATE ISSUED: Jun. 3, 1997
TITLE: Method of reducing TNF.alpha. levels with amino substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxo-and 1,3-dioxoisoindolines
INVENTOR: George W. Muller, Bridgewater, NJ
David I. Stirling, Branchburg, NJ
Roger S. -C. Chen, Edison, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/690,258
DATE FILED: Jul. 24, 1996
ART-UNIT: 123
PRIM-EXMR: C. Warren Ivy
ASST-EXMR: C. S. Aulakh
LEGAL-REP: Mathews, Collins, Shepherd & Gould, P.A.

US PAT NO: 5,635,517 [IMAGE AVAILABLE] L15: 58 of 72
US-CL-CURRENT: **514/323**; 546/201

SUMMARY:

BSUM(11)

The **nuclear** **factor** .**kappa**.**B** (NF.**kappa**.B) is a

pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,629,152 [IMAGE AVAILABLE] L15: 59 of 72
DATE ISSUED: May 13, 1997
TITLE: Trisubstituted .beta.-lactams and oligo .beta.-lactamamides
INVENTOR: Vasulinga Ravikumar, Carlsbad, CA
ASSIGNEE: Isis Pharmaceuticals, Inc., Carlsbad, CA (U.S. corp.)
APPL-NO: 08/283,591
DATE FILED: Aug. 1, 1994
ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
ASST-EXMR: Dianne Rees
LEGAL-REP: Woodcock Washburn Kurtz MacKiewicz & Norris

US PAT NO: 5,629,152 [IMAGE AVAILABLE] L15: 59 of 72
US-CL-CURRENT: 435/6, 91.1; **514/44**; 536/24.3, 24.5

DETDESC:

DETD(125)

Phosphorothioate . . . (Waters, Division of Millipore Corp., Milford, Ma.) and ethanol precipitated. The phosphorothioate oligonucleotides are hybridized to create the double stranded **NF**-**kB** binding site.

DETDESC:

DETD(129)

C-rel has been shown to represent a constituent of the **NF**-**kB** site binding transcription factor, which plays a crucial role in the expression of a number of genes including the immunoglobulin. . .

DETDESC:

DETD(130)

Crude . . . of poly dI.dC as a nonspecific competitor at a concentration of 100 .mu.g/ml of extract. Nuclear extracts containing the biotinylated **NF**-**kB** binding site competitor are prepared as in Example 34, above.

DETDESC:

DETD(131)

A series of oligo .beta.-lactamamide duplexes is synthesized to correspond to various length fragments of the consensus binding sequence of c-rel. **NF**-**kB** binding site competitor is added to each duplex and the resulting samples are washed. Antibody directed to rel is added.. . .

US PAT NO: 5,624,912 [IMAGE AVAILABLE] L15: 60 of 72
DATE ISSUED: Apr. 29, 1997
TITLE: Method of treating HIV infection and related secondary infections with defibrotide
INVENTOR: Arsinur Burcoglu, 213 Sweetgum Rd., Pittsburg, PA 15238
Marc Wagner, 4201 Greensburg Pike, Pittsburg, PA 15221
APPL-NO: 08/185,416
DATE FILED: Jan. 24, 1994
ART-UNIT: 189
PRIM-EXMR: Deborah Crouch
LEGAL-REP: Banner & Witcoff, Ltd.

US PAT NO: 5,624,912 [IMAGE AVAILABLE] L15: 60 of 72
US-CL-CURRENT: **514/44**, **924**, **934**

DETDESC:

DETD(118)

The transcription factor **NF**-**kB** binds to both the HIV-I enhancer, and the sILR2 gene. Protein kinase C phosphorylates its inhibitor IkB and releases active **NF**-**kB**. Increased cAMP levels by inhibiting directly the Ca.sup.2+ induced activation of protein kinase C would modulate this phosphorylation event, and downregulate the transcriptional activities related to **NF**-**kB**. Since **NFkB** binds to both the HIV enhancer and IL2 receptor, increased cAMP levels will downregulate HIV-I replication.

DETDESC:

DETD(138)
m) defibrotide sequence+LTR **NFkB** mutant (-104 to -80),

US PAT NO: 5,612,330 [IMAGE AVAILABLE] L15: 61 of 72
DATE ISSUED: Mar. 18, 1997
TITLE: Methods for inhibiting and controlling viral growth
INVENTOR: David T. Connor, Ann Arbor, MI
Stephen J. Gracheck, Ann Arbor, MI
ASSIGNEE: Warner-Lambert Company, Morris Plains, NJ (U.S. corp.)
APPL-NO: 08/408,431
DATE FILED: Mar. 22, 1995
ART-UNIT: 122
PRIM-EXMR: Robert T. Bond
LEGAL-REP: Charles W. Ashbrook

US PAT NO: 5,612,330 [IMAGE AVAILABLE] L15: 61 of 72
US-CL-CURRENT: **514/211**, **220**; 540/495

SUMMARY:

BSUM(7)

An . . . further development is therapeutic targeting along cellular signaling pathways that result in HIV-1 transcriptional activation. Among the potential targets is **nuclear** **factor**-.**kappa**.**B** (NF-.**kappa**.B), a transcriptional enhancer important for HIV-1 activation. In resting cells, preformed NF-.kappa.B exists in the cytoplasm bound to its inhibitor. . .

US PAT NO: 5,605,914 [IMAGE AVAILABLE] L15: 62 of 72
DATE ISSUED: Feb. 25, 1997
TITLE: Imides
INVENTOR: George W. Muller, Bridgewater, NJ
ASSIGNEE: Celgene Corporation, Warren, NJ (U.S. corp.)
APPL-NO: 08/258,587
DATE FILED: Jun. 10, 1994
ART-UNIT: 123
PRIM-EXMR: C. Warren Ivy
ASST-EXMR: D. Margaret M. Mach
LEGAL-REP: Mathews, Woodbridge & Collins

US PAT NO: 5,605,914 [IMAGE AVAILABLE] L15: 62 of 72
US-CL-CURRENT: **514/339**, **417**; 546/277.1; 548/465, 479

SUMMARY:

BSUM(14)

The **nuclear** **factor** kB (NF.**kappa**.**B**) is a pleiotropic transcriptional activator (Lenardo, et al. Cell 1989, 58, 227-29). NF.kappa.B has been implicated as a transcriptional activator. . .

US PAT NO: 5,596,011 [IMAGE AVAILABLE] L15: 63 of 72
DATE ISSUED: Jan. 21, 1997
TITLE: Method for the treatment of macular degeneration
INVENTOR: Karen M. Repine, 2275 Cherry Hills Farm Dr., Englewood, CO 80110
John E. Repine, 2275 Cherry Hills Farm Dr., Englewood, CO 80110
APPL-NO: 08/418,645
DATE FILED: Apr. 6, 1995
ART-UNIT: 125
PRIM-EXMR: Zohreh Fay

US PAT NO: 5,596,011 [IMAGE AVAILABLE] L15: 63 of 72
US-CL-CURRENT: **514/369**, **562**, **665**, **912**

DETDESC:

DETD(4)

As . . . protective mechanisms offered by N-acetylcysteine (NAC) include: scavenging (inactivation of) oxygen radicals (e.g. H.sub.2 O.sub.2, HOCl or .circle-solid.OH) directly; inhibiting **NFkB** nuclear factor activation, which is a known link between viral infection and activation of oxidative processes; decreasing oxidant-induced lipid peroxidation. . .

US PAT NO: 5,583,155 [IMAGE AVAILABLE] L15: 64 of 72
DATE ISSUED: Dec. 10, 1996
TITLE: 6-amino-1,2-benzopyrones useful for treatment of viral diseases
INVENTOR: Ernest Kun, Mill Valley, CA
Laure Aurelian, Baltimore, MD
ASSIGNEE: Octamer, Inc., Mill Valley, CA (U.S. corp.)
APPL-NO: 08/237,969
DATE FILED: May 3, 1994
ART-UNIT: 125
PRIM-EXMR: T. J. Criares

LEGAL-REP: Albert P. Halluin, Scott R.Pennie & Edmonds Bortner

US PAT NO: 5,583,155 [IMAGE AVAILABLE] L15: 64 of 72
US-CL-CURRENT: **514/457**, **456**

DETDESC:

DETD(42)

Expression . . . by phorbol esters and lectins as described in Science, 108:117 (1948); and Ibid, 230:850 (1986). This stimulation is mediated by **NF**-**kB**, a factor that regulates transcription and binds to the twice-repeated 11-bp kB motif in the HIV enhancer Nature, 326, 711 (1987). Mutations within this site that eliminate the binding of **NF**-**kB** also abolish the increase in HIV gene expression in activated T cells. However, HIV persists in macrophages in which it. .

DETDESC:

DETD(43)

AIDS . . . synthesized immediately after infection resulting in immediate-early gene products. These include the trans-activating genes that activate HIV-LTRcat involving induction of **NF**-**kB** activity. CMV also activates HIV expression. This is mediated by the CMV IE gene. However, it does not appear to require **NF**-**kB** activity.

US PAT NO: 5,571,797 [IMAGE AVAILABLE] L15: 65 of 72
DATE ISSUED: Nov. 5, 1996
TITLE: Method of inducing gene expression by ionizing radiation
INVENTOR: Tsuneya Ohno, Boston, MA
Ralph R. Weichselbaum, Chicago, IL
Donald W. Kufe, Wellesley, MA
ASSIGNEE: Arch Development Corporation, Chicago, IL (U.S. corp.)
APPL-NO: 08/241,863
DATE FILED: May 11, 1994
ART-UNIT: 184
PRIM-EXMR: Bruce R. Campell
LEGAL-REP: Arnold White & Durkee

US PAT NO: 5,571,797 [IMAGE AVAILABLE] L15: 65 of 72
US-CL-CURRENT: **514/44**; 424/1.11, 1.49, 1.61, 1.65, 1.69, 93.2, 93.21, 450; 435/69.1, 69.5, 320.1; 536/24.1

DETDESC:

DETD(79)

Transcription . . . domains are well known in the art. Exemplary transcription factors having activation domains are GAL4, c-Jun, viral protein VP-16, and **nuclear** **factor** NF-.**kappa**.**B**.

DETDESC:

DETD(94)

Nuclear **factor** NF-.**kappa**.**B** is a transcription factor. The activation domain of NF-.kappa.B comprises amino acid residue sequences from about residue position 414 to. . .

DETDESC:

DETD(270)

The . . . al., 1990; Hallahan, et al, 1991). Other studies have demonstrated that x-rays induce expression and DNA binding activity of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B; Brach, et al., 1991).

DETDESC:

DETD(313)

Ionizing . . . which code for transcription factors. Other studies have demonstrated that ionizing radiation induces expression and DNA binding activity of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B). The activation of transcription factors likely represents a critical control point in transducing early nuclear signals to longer term changes. . .

DETDESC:

DETD(328)

NAC . . . phorbol ester-induced activation of the HIV-1 long terminal repeat. This antioxidant has also been found to inhibit activation of the **nuclear** **factor** .**kappa**.**B** (NF-.**kappa**.B) by phorbol esters and other agents such as H.sub.2 O.sub.2. The available findings suggest that ROIs activate NF-.kappa.B by induced. . .

US PAT NO: 5,550,132 [IMAGE AVAILABLE] L15: 66 of 72
DATE ISSUED: Aug. 27, 1996
TITLE: Hydroxyalkylammonium-pyrimidines or purines and nucleoside derivatives, useful as inhibitors of inflammatory cytokines
INVENTOR: Bradley J. Benson, Chapel Hill, NC
Xiannong Chen, Athens, GA
George J. Cianciolo, Chapel Hill, NC
Jose-Luis Diaz, Durham, NC
Khalid S. Ishaq, Chapel Hill, NC
Susan L. Morris-Natschke, Apex, NC
Ronald J. Uhing, Durham, NC
Henry Wong, Morrisville, NC
ASSIGNEE: University of North Carolina, Chapel Hill, NC (U.S. corp.)
Macronex, Inc., Morrisville, NC (U.S. corp.)
APPL-NO: 08/264,026
DATE FILED: Jun. 22, 1994
ART-UNIT: 122
PRIM-EXMR: Yogendra N. Gupta
LEGAL-REP: Klauber & Jackson

US PAT NO: 5,550,132 [IMAGE AVAILABLE] L15: 66 of 72
US-CL-CURRENT: **514/269**, **274**; 544/311, 312, 313, 314

SUMMARY:

BSUM(3)

Two . . . that they employ different signal transduction pathways. While both receptors are capable of binding TNF and activating the transcription factor **NFkB**, it appears that the expression of each receptor is independently and differentially regulated. Human TNF-.alpha. will bind to both types. . .

US PAT NO: 5,547,979 [IMAGE AVAILABLE] L15: 67 of 72
DATE ISSUED: Aug. 20, 1996
TITLE: TNF inhibition
INVENTOR: Siegfried B. Christensen, IV, Philadelphia, PA
Klaus M. Esser, Downingtown, PA
Philip L. Simon, Randolph, NJ
ASSIGNEE: SmithKline Beecham, Philadelphia, PA (U.S. corp.)
APPL-NO: 08/424,944
DATE FILED: Apr. 19, 1995
ART-UNIT: 121
PRIM-EXMR: David B. Springer
LEGAL-REP: Dara L. Dinner, Stephen Venetianer, Edward T. Lentz

US PAT NO: 5,547,979 [IMAGE AVAILABLE] L15: 67 of 72
US-CL-CURRENT: **514/424**; 548/550, 551

DETDESC:

DETD(29)

There . . . (1989)]. A molecular mechanism for the virus inducing activity is suggested by TNFs ability to activate a gene regulatory proteins (**NF**-**kB**) found in the cytoplasm of cells, which promotes HIV replication through binding to a viral regulatory gene sequence (LTR) [See,. . .

US PAT NO: 5,420,154 [IMAGE AVAILABLE] L15: 68 of 72
DATE ISSUED: May 30, 1995
TITLE: TNF inhibitors
INVENTOR: Siegfried B. Christensen, IV, Philadelphia, PA
Klaus M. Esser, Downingtown, PA
Philip L. Simon, Randolph, NJ
ASSIGNEE: SmithKline Beecham Corp., Philadelphia, PA (U.S. corp.)
APPL-NO: 07/852,180
DATE FILED: Mar. 30, 1992
ART-UNIT: 121
PRIM-EXMR: David B. Springer
LEGAL-REP: Dara L. Dinner, Stephen Venetianer, Edward T. Lentz

US PAT NO: 5,420,154 [IMAGE AVAILABLE] L15: 68 of 72
US-CL-CURRENT: **514/424**; 548/551

DETDESC:

DETD(29)

There . . . (1989)]. A molecular mechanism for the virus inducing activity is suggested by TNFs ability to activate a gene regulatory protein (**NF**-**kB**) found in the cytoplasm of cells, which promotes HIV replication through binding to a viral regulatory gene sequence (LTR) [See,. . .

US PAT NO: 5,380,747 [IMAGE AVAILABLE] L15: 69 of 72
DATE ISSUED: Jan. 10, 1995
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
ASSIGNEE: Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 07/969,934
DATE FILED: Oct. 30, 1992
ART-UNIT: 125
PRIM-EXMR: Marianne M. Cintins
ASST-EXMR: William R. Jarvis
LEGAL-REP: Kilpatrick & Cody

US PAT NO: 5,380,747 [IMAGE AVAILABLE] L15: 69 of 72
US-CL-CURRENT: **514/423**, **210**, **212**, **315**, **476**, **477**

DETDESC:

DETD(28)

At the molecular level, PDTC has been shown to inhibit the activation of the transcriptional regulatory factor **Nf**-**kB** in response to certain cytokine and non-cytokine stimuli (Schreck, Rieber et al. 1991; Schreck, Meier et al. 1992). However, by. . . has been discovered that endothelial cells activate VCAM-1 gene expression through an apparently novel transcriptional regulatory factor that is not **Nf**-**kB**. This suggests that PDTC may regulate endothelial cell gene expression through its effect on a new transcriptional regulatory protein. It. . .

US PAT NO: 5,317,019 [IMAGE AVAILABLE] L15: 70 of 72
DATE ISSUED: May 31, 1994
TITLE: Inhibition of interleukin-1 and tumor necrosis factor production by monocytes and/or macrophages
INVENTOR: Paul E. Bender, Cherry Hill, NJ
Don E. Griswold, North Wales, PA
Nabil Hanna, Solana Beach, CA
John C. Lee, Radnor, PA
Bartholomew J. Votta, Pottstown, PA
Philip L. Simon, Randolph, NJ
Alison M. Badger, Bryn Mawr, PA
Klaus M. Esser, Downingtown, PA
ASSIGNEE: SmithKline Beecham Corp., Phildelphia, PA (U.S. corp.)
APPL-NO: 07/809,484
DATE FILED: Dec. 12, 1991
ART-UNIT: 123
PRIM-EXMR: C. Warren Ivy
ASST-EXMR: Raymond Covington
LEGAL-REP: Dara L. Dinner, Stephen Venetianer, Edward T. Lentz

US PAT NO: 5,317,019 [IMAGE AVAILABLE] L15: 70 of 72
US-CL-CURRENT: **514/224.2**, **230.5**, **258**, **303**, **333**, **338**, **339**

SUMMARY:

BSUM(366)

There . . . (1989)]. A molecular mechanism for the virus inducing activity is suggested by TNFs ability to activate a gene regulatory protein (**NF**-**kB**) found in the cytoplasm of cells, which promotes HIV replication through binding to a viral regulatory gene sequence (LTR) [See,. . .

US PAT NO: 5,306,724 [IMAGE AVAILABLE] L15: 71 of 72
DATE ISSUED: Apr. 26, 1994
TITLE: Method for preventing and treating atherosclerosis
INVENTOR: Dennis I. Goldberg, Palatine, IL
ASSIGNEE: Clintec Nutrition Company, Deerfield, IL (U.S. corp.)
APPL-NO: 07/930,183
DATE FILED: Aug. 17, 1992
ART-UNIT: 125
PRIM-EXMR: Frederick E. Waddell
ASST-EXMR: William R. A. Jarvis
LEGAL-REP: Hill, Steadman & Simpson

US PAT NO: 5,306,724 [IMAGE AVAILABLE] L15: 71 of 72
US-CL-CURRENT: **514/369**, **824**

SUMMARY:

BSUM(30)

Adhesion . . . and growth factors which exacerbate the injury. The inflammatory process is promoted by cytokine activation of nuclear transcription factor kB (**NF**-**kB**). This transcription factor is known to control the expression of a number of genes that code for cytokines and other. . .

SUMMARY:

BSUM(32)

Intracellular free radicals and hydrogen peroxides may serve as second messengers, transducing the cytokine signal to activate **NF**-**kB**. The activation of **NF**-**kB** by a variety of pro-inflammatory cytokines, including interleukin-1. Lipopolysaccharide, lectin, TNF-.alpha., phorbol ester and calcium ionophore, can be blocked by thiol containing compounds. Elevation of intracellular glutathione levels has been demonstrated to prevent the induction of HIV replication by **NF**-**kB**. The inventor believes that this data supports the hypothesis that maintaining intracellular glutathione levels may prevent the induction of proinflammatory. . .

US PAT NO: 5,294,630 [IMAGE AVAILABLE] L15: 72 of 72
DATE ISSUED: Mar. 15, 1994
TITLE: Treatment of inflammatory bowel disease
INVENTOR: David Blake, Droitwich, United Kingdom
Peter P. K. Ho, Carmel, IN
Jill A. Panetta, Zionsville, IN
David Rampton, London, United Kingdom
Nicola Simmonds, London, United Kingdom
ASSIGNEE: Eli Lilly and Company, Indianapolis, IN (U.S. corp.)
London Hospital Medical College, London, England (foreign corp.)
APPL-NO: 07/909,852
DATE FILED: Jul. 7, 1992
ART-UNIT: 125
PRIM-EXMR: Leonard Schenkman
LEGAL-REP: Joseph A. Jones, Leroy Whitaker

US PAT NO: 5,294,630 [IMAGE AVAILABLE] L15: 72 of 72
US-CL-CURRENT: **514/372**, **378**, **380**, **403**, **404**

SUMMARY:

BSUM(8)

The . . . inflammatory cascade which leads to IBD. Schreck, Reactive Oxygen Intermediates, as Apparently Widely Used Messengers in the Activation of the **NF**-**KB** transcription factor and HIV-1, EMBO Journal 10, 2247-58 (1991).